"Primary Abstract","Primary Paper","Secondary Abstract","Secondary Paper","Duplicate","Have PDF","Year","Author","Title","Journal","Issue","Id","DuplicateOf","Abstract","Primary Comment","Secondary Comment","Source","pmid","pub_date","pub_affiliation","pub_authorlang","pub_journal","pub_journalshort","pub_place","pub_type","pub_issn"
"Unknown","Unknown","Unknown","Unknown","","","2008","Abdalla, H., Matambo, T. S., Koekemoer, L. L., Mnzava, A. P., Hunt, R. H., Coetzee, M.","Insecticide susceptibility and vector status of natural populations of Anopheles arabiensis from Sudan","Transactions of the Royal Society of Tropical Medicine and Hygiene","102(3):263-71","2b11236f-cd80-4cb1-b935-04d9860f16a8","","Species composition, blood meal source, sporozoite infection rate, insecticide resistance and the kdr mutations were investigated in the Anopheles gambiae complex from 13 sentinel sites in central Sudan. Species identification revealed that 89.5% of 960 specimens were A. arabiensis. Of 310 indoor resting females, 88.1% were found to have fed on humans, while 10.6% had fed on bovines. The overall sporozoite infection rate from the five localities tested was 2.3%, ranging from 0 to 5.5%. Insecticide susceptibility bioassay results showed 100% mortality on bendiocarb, 54.6-94.2% on permethrin, 55.4-99.1% on DDT and 76.8-100% on malathion. The kdr analysis by PCR and sequencing revealed the presence of the Leu-Phe mutation in both permethrin and DDT bioassays. There was no significant difference in the frequency of kdr (P>0.05) between dead and surviving specimens. These findings have serious implications for the malaria control programmes in Gezira and Sennar states.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","2011","Aboul-Soud, M. A., Al-Othman, A. M., El-Desoky, G. E., Al-Othman, Z. A., Yusuf, K., Ahmad, J., Al-Khedhairy, A. A.","Hepatoprotective effects of vitamin E/selenium against malathion-induced injuries on the antioxidant status and apoptosis-related gene expression in rats","The Journal of toxicological sciences","36(3):285-96","a3dd909a-8cb2-40c8-ab8a-68aec4941e09","","The present study is undertaken to evaluate the protective effect of vitamin E (alpha-tocopherol) and selenium (Se) against malathion (MTN)-induced oxidative stress and hepatic injuries in experimental rats. Male rats were randomly divided into eight groups comprised of 10 rats each. The 1(st) group served as a negative control (C(N)), whereas the 2(nd) was supplemented with a combination of alpha-tocopherol (100 mg kg(-1) body weight, b.w.)/Se (0.1 mg kg(-1) bw). The 3(rd), 4(th) and 5(th) groups were respectively administered with increasing doses of MTN equivalent to (1/50)LD(50) (M(1/50)), (1/25) LD(50) (M(1/25)) and (1/10) LD(50) (M(1/10)), respectively. The 6(th), 7(th) and 8(th) groups were administered the same doses of MTN as in the 3(rd), 4(th) and 5(th) groups with a concomitant supplementation with alpha-tocopherol/Se. Subchronic exposure of rats to MTN for 45 days resulted in statistical dose-dependent decrease in acetylcholinestrase (AChE) activity, increase in oxidative stress marker lipid peroxidation (LPO) and reduction in reduced glutathione (GSH) level. Moreover, the levels of glutathione persoxidase (GPx), superoxide dismutase (SOD) and catalase (CAT) were significantly decline in response to MTN exposure in a dose-dependent fashion. Furthermore, histopathological studies of liver in the rats which received MTN exhibited, moderate to severe degenerative and necrotic changes in the hepatocytes. Notably, the administration of alpha-tocopherol/Se protected the liver of rats exposed to MTN as evidenced by the appearance of normal histological structures, significant attenuation of the decline in all antioxidant

enzymes tested (i.e. GPx, SOD and CAT), significant recovery in the GSH level and statistical reduction in LPO, as compared to the experimental rat. The effect of alpha-tocopherol/Se supplementation on transcriptional activity of three key stress and apoptosis-related genes (i.e., Tp53, CASP3 and CASP9), in response to MTN exposure in rats, was investigated. Results revealed a significant concentration-dependent up-regulation in the level of expression for the three genes examined, in response to MTN exposure, compared with the control. Interestingly, the supplementation of MTN-treated rats with alpha-tocopherol/Se modulates the observed significant dose-dependent up-regulation in the level of expression for three selected genes, indicative of an interfering role in the signaling transduction process of MTN-mediated poisoning. Taken together, these data suggest that the administration of alpha-tocopherol/Se may partially protect against MTN-induced hepatic oxidative stress and injuries.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","2016","Ahmad, M., Buhler, C., Pignatelli, P., Ranson, H., Nahzat, S. M., Naseem, M., Sabawoon, M. F., Siddiqi, A. M., Vink, M.","Status of insecticide resistance in high-risk malaria provinces in Afghanistan","Malaria journal","15(1):98","0566b1f4-cce2-4077-a55c-31b70a4a3e81","","BACKGROUND: Insecticide resistance seriously threatens the efficacy of vector control interventions in malaria endemic countries. In Afghanistan, the status of insecticide resistance is largely unknown while distribution of long-lasting insecticidal nets has intensified in recent years. The main objective of this study was thus to measure the level of resistance to four classes of insecticides in provinces with medium to high risk of malaria transmission. METHODS: Adult female mosquitoes were reared from larvae successively collected in the provinces of Nangarhar, Kunar, Badakhshan, Ghazni and Laghman from August to October 2014. WHO insecticide susceptibility tests were performed with DDT (4 %), malathion (5 %), bendiocarb (0.1 %), permethrin (0.75 %) and deltamethrin (0.05 %). In addition, the presence of kdr mutations was investigated in deltamethrin resistant and susceptible Anopheles stephensi mosquitoes collected in the eastern provinces of Nangarhar and Kunar. RESULTS: Analyses of mortality rates revealed emerging resistance against all four classes of insecticides in the provinces located east and south of the Hindu Kush mountain range. Resistance is observed in both An. stephensi and Anopheles culicifacies, the two dominant malaria vectors in these provinces. Anopheles superpictus in the northern province of Badakhshan shows a different pattern of susceptibility with suspected resistance observed only for deltamethrin and bendiocarb. Genotype analysis of knock down resistance (kdr) mutations at the voltage-gated channel gene from An. stephensi mosquitoes shows the presence of the known resistant alleles L1014S and L1014F. However, a significant fraction of deltamethrin-resistant mosquitoes were homozygous for the 1014L wild type allele indicating that other mechanisms must be considered to account for the observed pyrethroid resistance. CONCLUSIONS: This study confirms the importance of monitoring insecticide resistance for the development of an integrated vector management in Afghanistan. The validation of the kdr genotyping PCR assay applied to An. stephensi collected in Afghanistan paves the way for further studies into the mechanisms of insecticide resistance of malaria vectors in this region.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","2011","Ahmed, T., Pathak, R., Mustafa, M., Kar, R., Tripathi, A. K., Ahmed, R. S., Banerjee, B. D.","Ameliorating effect of N-acetylcysteine and curcumin on pesticide-induced oxidative DNA damage in human

peripheral blood mononuclear cells","","179(1-4):293-299","b168fe55-73de-4bdd-9ee2-cfc57c702a9d","","Endosulfan, malathion, and phosphamidon are widely used pesticides. Subchronic exposure to these contaminants commonly affects the central nervous system, immune, gastrointestinal, renal, and reproductive system. There effects have been attributed to increased oxidative stress. This study was conducted to examine the role of oxidative stress in genotoxicity following pesticide exposure using peripheral blood mononuclear cells (PBMC) in vitro. Further possible attenuation of genotoxicity was studied using N-acetylcysteine (NAC) and curcumin as known modulators of oxidative stress. Cultured mononuclear cells was isolated from peripheral blood of healthy volunteers, and exposed to varying concentrations of different pesticides: endosulfan, malathion, and phosphamidon for 6, 12, and 24 h. Lipid peroxidation was assessed by cellular malondialdehyde (MDA) level and DNA damage was quantified by measuring 8-hydroxy-2'-deoxyguanosine (8-OH-dG) using ELISA. Both MDA and 8-OH-dG were significantly increased in a dose-dependent manner following treatment with these pesticides. There was a significant decrease in MDA and 8-OH-dG levels in PBMC when co-treated with NAC or/and curcumin as compared to pesticide alone. These results indicate that pesticide-induced oxidative stress is probably responsible for the DNA damage, and NAC or curcumin attenuate this effect by counteracting the oxidative stress. Â© 2010 Springer Science+Business Media B.V.","","","RefMan","","","","","","","","","","Unknown","Unknown","Unknown","Unknown","","","2013","Alavanja, M. C. R., Ross, M. K., Bonner, M. R.","Reply to Increased cancer burden among pesticide applicators and others due to pesticide exposure","","63(5):366-367","d3049b42-29ae-4b10-afe0-feb7db22ecd8","","","","","RefMan","","","","","","","","","","Unknown","Unknown","Unknown","Unknown","","","2013","Alavanja, M. C. R., Ross, M. K., Bonner, M. R.","Increased cancer burden among pesticide applicators and others due to pesticide exposure","","63(2):120-142","4f669433-41a1-48e3-996e-8f854c88b6c0","","A growing number of well-designed epidemiological and molecular studies provide substantial evidence that the pesticides used in agricultural, commercial, and home and garden applications are associated with excess cancer risk. This risk is associated both with those applying the pesticide and, under some conditions, those who are simply bystanders to the application. In this article, the epidemiological, molecular biology, and toxicological evidence emerging from recent literature assessing the link between specific pesticides and several cancers including prostate cancer, non-Hodgkin lymphoma, leukemia, multiple myeloma, and breast cancer are integrated. Although the review is not exhaustive in its scope or depth, the literature does strongly suggest that the public health problem is real. If we are to avoid the introduction of harmful chemicals into the environment in the future, the integrated efforts of molecular biology, pesticide toxicology, and epidemiology are needed to help identify the human carcinogens and thereby improve our understanding of human carcinogenicity and reduce cancer risk. Â© 2013 American Cancer Society, Inc.","","","RefMan","","","","","","","","","","Unknown","Unknown","Unknown","Unknown","","","2008","Aldana-Madrid, M. L., Valdez-Hurtado, S., Vargas-Valdez, N. D., Salazar-Lopez, N. J., Silveira-Gramont, M. I., Loarca-PiÃ±a, F. G., RodrÃguez-Olibarria, G., Wong-Corral, F. J., Borboa-Flores, J., Burgos-HernÃ¡ndez, A.","Insecticide residues in stored grains in Sonora, Mexico: Quantification and toxicity testing","","80(2):93-96","59545a54-922c-4afe-abb2-0d7679d644f4","","Food safety has acquired great attention by food importer and exporters. Food rejection or acceptance across international borders is based on the

compliance with international food regulations. Due to the lack of recent data on pesticide residues in Mexican grains, this study focused on detecting and quantifying insecticide residues in stored wheat, corn, chickpeas, and beans, as well as to determine their mutagenic potential. Grains were sampled from primary storage sites in Sonora, Mexico. Malathion, chlorpyrifos, deltamethrin, cypermethrin, 4,4-DDE, 4,4-DDD and 4,4-DDT were analyzed in 135 samples. Grain samples were not mutagenic and most pesticide levels were within regulation limits. Â© 2008 Springer Science+Business Media, LLC.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","2005","Aleem, A., Malik, A.","Genotoxicity of the Yamuna River water at Okhla (Delhi), India","Ecotoxicology and environmental safety","61(3):404-12","585e21bf-e3b9-4462-8d6f-72b4773ffee4","","Water samples from the Yamuna River at Okhla (Delhi), India, were concentrated using XAD resins (XAD-4 and XAD-8) and liquid-liquid extraction procedures. Gas chromatographic analysis of liquid-liquid extracted water samples revealed the presence of the pesticides DDT, BHC, dieldrin, endosulfan, aldrin, 2,4-D, dimethoate, methyl parathion, and malathion at concentrations of 14, 25, 2.1, 114, 0.9, 0.6, 0.9, 1.7, and 1.9 ng/L, respectively. The genotoxicity of the extracted water samples was evaluated with the Ames Salmonella/mammalian microsome test, DNA repair-defective mutants, and bacteriophage lambda systems. The results of the Salmonella test demonstrated that the XAD-concentrated water samples had maximum mutagenicity with the TA98 strain both with and without metabolic activation. However, the liquid-liquid-extracted water samples were also found to be mutagenic with one or more of the Ames tester strains, but to a lesser extent as compared with XAD extracts. The damage brought about in the DNA repair-defective mutants in the presence of XAD-concentrated water samples was found to be markedly high as compared with that liquid-liquid-extracted water samples at the dose level of 20 microl/mL culture. All mutants invariably exhibited significant declines in their colony-forming units as compared with their isogenic wild-type counterparts. Survival decreased by 86.3 and 75.5% in the polA- strain after 6 h of treatment with XAD-concentrated and liquid-liquid-extracted water samples, respectively. A significant decrease was also observed in the survival of bacteriophage lambda when treated with the test samples. Mutagenic responses of the liquid-liquid-extracted water samples may not necessarily reflect the mutagenicity of existing pesticides in the test water, because some other organic pollutants might accompany the pesticides in the extract.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","2002","Amer, S. M., Fahmy, M. A., Aly, F. A., Farghaly, A. A.","Cytogenetic studies on the effect of feeding mice with stored wheat grains treated with malathion","Mutation research","513(1-2):1-10","88e46047-42a7-41a7-8efe-ab7df03d6c28","","The cytogenetic effect of malathion residues in wheat grains stored for different periods of time (4, 12, 24 weeks) was evaluated in Swiss mice. The studies included: (1) chromosomal aberrations analysis in bone-marrow and spermatocyte cells; (2) chromosomal aberrations and sister chromatid exchange (SCE) analysis in spleen cell culture from mice fed with stored wheat grains. The tested doses were 8.36 (applied dose), 25.08 and 41.80 mg malathion kg(-1) wheat grains. The results demonstrated that the cytogenetic effect induced in different mouse tissues by malathion residues was dose-dependent and increased with increasing of both feeding and storage periods. Feeding mice with wheat grains stored for 4 weeks had a non-significant effect with respect to the induction of chromosomal aberrations or SCEs. Significant chromosome damage and increase of SCEs were observed in mice fed with wheat

grains stored for 12 weeks. The maximum effect was recorded in mice fed for 12 weeks with the grains treated with the highest tested dose and stored for 24 weeks. However, mitomycin C i.p.-injected in mice at 1 mg kg(-1) body weight (b.w.) (positive control) induced a higher effect. The percentage of chromosome aberrations reached 13.60+/-0.98, 13.60+/-0.77 and 11.73+/-0.98 (P<0.01) in bone-marrow, cultured spleen cells and spermatocytes, respectively. The significant increase of abnormalities in spermatocytes was seen for univalent formation only, predominantly of the sex chromosomes. The frequency of SCEs was 10.76+/-0.62 per cell (P<0.01) in cultured spleen cells compared with 5.46+/-0.45 per cell for control and 14.66+/-0.54 per cell for the positive control. The obtained results indicate that malathion residues in stored wheat grains have potential genotoxic effect in mice under the conditions tested.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","1996","Amer, S. M., Fahmy, M. A., Donya, S. M.","Cytogenetic effect of some insecticides in mouse spleen","Journal of applied toxicology : JAT","16(1):1-3","eb5314b4-ed2c-45b3-8b7f-feb011a2b3f5","","Several insecticides were tested for their ability to induce chromosomal aberrations in mouse spleen. They were injected i.p. in doses representing approximately 1/8-1/10 of the respective LD50 values. Doses were: DDT, 5.5 mg kg-1 body wt.; malathion, 30 mg kg-1 body wt.; Dursban, 4 mg kg-1 body wt.; Sevin, 7 mg kg-1 body wt.; and Lannate, 1 mg kg-1 body wt. 'Mitomycin C' at a dose of 1 mg kg-1 body wt. was used as a positive control. Mice were sacrificed 6, 24 and 48 h after treatment. DDT, malathion, dursban and lannate caused maximum chromosomal aberrations 24 h after injection, whereas Sevin induced its maximum effect 6 h after the treatment. All the insecticides induced statistically significant chromosomal aberrations even after excluding the number of metaphases with gaps. The results indicate genotoxicity in mouse spleen cells.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","2013","Angelini, D. J., Dorsey, R. M., Willis, K. L., Hong, C., Moyer, R. A., Oyler, J., Jensen, N. S., Salem, H.","Chemical warfare agent and biological toxin-induced pulmonary toxicity: Could stem cells provide potential therapies?","","25(1):37-62","aa1f67f2-fc96-4222-85eb-959c1b10cec2","","Chemical warfare agents (CWAs) as well as biological toxins present a significant inhalation injury risk to both deployed warfighters and civilian targets of terrorist attacks. Inhalation of many CWAs and biological toxins can induce severe pulmonary toxicity leading to the development of acute lung injury (ALI) as well as acute respiratory distress syndrome (ARDS). The therapeutic options currently used to treat these conditions are very limited and mortality rates remain high. Recent evidence suggests that human stem cells may provide significant therapeutic options for ALI and ARDS in the near future. The threat posed by CWAs and biological toxins for both civilian populations and military personnel is growing, thus understanding the mechanisms of toxicity and potential therapies is critical. This review will outline the pulmonary toxic effects of some of the most common CWAs and biological toxins as well as the potential role of stem cells in treating these types of toxic lung injuries. Â© 2013 Informa Healthcare USA, Inc.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","2013","Anjum, R., Malik, A.","Evaluation of mutagenicity of wastewater in the vicinity of pesticide industry","Environmental toxicology and pharmacology","35(2):284-91","d891af6f-3a88-45e8-b9e7-b47ef3b25dd3","","Pesticide industrial wastewater samples were taken from the Chinhat

industrial area nearby Lucknow city, India. GC-MS analysis revealed the presence of pesticides lindane, alpha-endosulfan, beta-endosulfan, chlorpyriphos, monocrotophos, dimethoate and malathion. A pesticide mixture and wastewater extracts were studied to determine the mutagenicity by Ames Salmonella test, survival of DNA repair defective E. coli K-12 mutants and bacteriophage lambda systems. Wastewater samples were concentrated with XAD-resins as an adsorbent and liquid-liquid extraction procedure. The XAD concentrated sample exhibited maximum mutagenic activity in comparison to liquid-liquid extracted sample. TA98 strain was the most responsive strain for both test samples with (+S9) and without (-S9) metabolic activation, while other strains exhibited weak response. A significant decline of DNA repair defective E. coli K-12 mutants, bacteriophage lambda was observed with test samples in the survival. The intracellular damage was highest when treated with XAD concentrated sample as compared to liquid-liquid extract after 6h treatment.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","2009","Ansari, M. I., Malik, A.","Genotoxicity of agricultural soils in the vicinity of industrial area","Mutation research","673(2):124-32","3cc52653-1ceb-4ec2-afd6-2105f424c304","","Soil samples from agricultural fields (cultivated) in the vicinity of industrial area of Ghaziabad City (India) were collected. In this city, wastewater coming from both industrial and domestic sources and without any treatment is used to irrigate the food crops. This practice has been polluting the soil and pollutants might reach the food chain. Gas chromatographic analysis show the presence of certain organochlorine (DDE, DDT, dieldrin, aldrin and endosulfan) and organophosphorus (dimethoate, malathion, methylparathion and chlorpyrifos) pesticides in soil samples. Samples were extracted using different solvents, i.e. methanol, chloroform, acetonitrile, hexane and acetone (all were HPLC-grade, SRL, India), and the extracts were assayed for genotoxic potential using Ames Salmonella/microsome test, DNA repair defective mutants and bacteriophage lambda systems. TA98 and TA100 were found to be the most sensitive strains to all the soil extracts tested. Methanol extracts exhibited a maximum mutagenicity with TA98 strain {540 (-S9) and 638 (+S9) revertants/g of soil} and 938 (-S9) and 1008 (+S9) revertants/g of soil with TA100 strain. The damage in the DNA repair defective mutants was found maximum with methanolic extract followed by acetonitrile, chloroform, hexane and acetone at the dose level of 40 microl/ml culture after 6h of treatment. The survival was 25, 30, 32, 33 and 35% in polA strain after 6h of treatment when tested with wastewater irrigated soil extracts of methanol, acetonitrile, chloroform, hexane and acetone, respectively. A significant decrease in the plaque forming units of bacteriophage lambda was also observed when treated with 40 microl of test samples. Present results showed that methanolic extracts of soil were more toxic than other soil extracts. The soil is accumulating a large number of pollutants due to wastewater irrigation and this practice of accumulation has an impact on soil health.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","2009","Ansari, M. I., Malik, A.","Genotoxicity of wastewaters used for irrigation of food crops","Environmental toxicology","24(2):103-15","ec861d27-2dda-4640-a90a-63cb7aaf23af","","In most towns of India, wastewater coming from both industrial and domestic sources and without any treatment is used to irrigate the agricultural crops. This practice has been polluting the soil, and pollutants could possibly reach the food chain. For the above reasons, the wastewaters of Ghaziabad City (India), which is used for irrigation, were sampled (at two different sites) and monitored for the presence of genotoxic agents from

January 2005 to June 2007. Gas chromatographic analysis showed the presence of certain OC (DDE, DDT, Dieldrin, Aldrin, and Endosulfan) and OP (Dimethoate, Malathion, Methlyparathion, and Chlorpyrifos) pesticides in both the sampling sites. Wastewater samples were concentrated using XAD resins (XAD-4 and XAD-8) and liquid-liquid extraction procedures, and the extracts were assayed for genotoxic potential by Ames Salmonella/microsome test, DNA repair defective mutants, and bacteriophage lambda systems. The test samples exhibited significant mutagenicity with TA98, TA97a, and TA100 strains with the probable role of contaminating pesticides in the wastewater. However, XAD-concentrated samples were more mutagenic in both sites as compared to liquid-liquid-extracted samples. The damage in the DNA repair defective mutants in the presence of XAD-concentrated water samples were also found to be higher to that of liquid-liquid-extracted water samples at the dose level of 20 muL/mL culture. All the mutants invariably exhibited significant decline in their colony-forming units as compared to their isogenic wild-type counterparts. The survival was decreased by 81.7 and 75.5% in polA(-) strain in site I, and 76.0 and 73.5% in site II in polA(-) under the same experimental conditions after 6 h of treatment with XAD-concentrated and liquid-liquid-extracted samples, respectively. A significant decrease in the survival of bacteriophage lambda was also observed when treated with the test samples.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","2015","Arshad, M., Siddiqa, M., Rashid, S., Hashmi, I., Awan, M. A., Ali, M. A.","Biomonitoring of Toxic Effects of Pesticides in Occupationally Exposed Individuals","","","ed75b343-705a-4e85-bc41-9b2203983f7b","","Background: Workers in pesticide manufacturing industries are constantly exposed to pesticides. Genetic biomonitoring provides an early identification of potential cancer and genetic diseases in exposed populations. The objectives of this biomonitoring study were to assess DNA damage through comet assay in blood samples collected from industry workers and compare these results with those of classical analytical techniques used for complete blood count analysis. Methods: Samples from controls (n = 20) and exposed workers (n = 38) from an industrial area in Multan, Pakistan, were subjected to various tests. Malathion residues in blood samples were measured by gas chromatography. Results: The exposed workers who were employed in the pesticide manufacturing industry for a longer period (i.e., 13-25 years) had significantly higher DNA tail length (7.04 Î¼m) than the controls (0.94 Î¼m). Workers in the exposed group also had higher white blood cell and red blood cell counts, and lower levels of mean corpuscular hemoglobin (MCH), MCH concentration, and mean corpuscular volume in comparison with normal levels for these parameters. Malathion was not detected in the control group. However, in the exposed group, 72% of whole blood samples had malathion with a mean value of 0.14 mg/L (range 0.01-0.31 mg/L). Conclusion: We found a strong correlation (R 2 = 0.91) between DNA damage in terms of tail length and malathion concentration in blood. Intensive efforts and trainings are thus required to build awareness about safety practices and to change industrial workers' attitude to prevent harmful environmental and anthropogenic effects.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","2000","Bachmann, T. T., Leca, B., Vilatte, F., Marty, J. L., Fournier, D., Schmid, R. D.","Improved multianalyte detection of organophosphates and carbamates with disposable multielectrode biosensors using recombinant mutants of Drosophila acetylcholinesterase and artificial neural networks","Biosensors & bioelectronics","15(3-4):193-201","913e84be-8f1a-4cc5-866b-

51dba49f8b7c","","Engineered variants of Drosophila melanogaster acetylcholinesterase (AChE) were used as biological receptors of AChE-multisensors for the simultaneous detection and discrimination of binary mixtures of cholinesterase-inhibiting insecticides. The system was based on a combination of amperometric multielectrode biosensors with chemometric data analysis of sensor outputs using artificial neural networks (ANN). The multisensors were fully manufactured by screen-printing, including enzyme immobilisation. Two types of multisensors were produced that consisted of four AChE variants each. The AChE mutants were selected in order to obtain high resolution, enhanced sensitivity and minimal assay time. This task was successfully achieved using multisensor I equipped with wild-type Drosophila AChE and mutants Y408F, F368L, and F368H. Each of the AChE variants was selected on the basis of displaying an individual sensitivity pattern towards the target analytes. For multisensor II, the inclusion of F368W, which had an extremely diminished paraoxon sensitivity, increased the sensor's capacity even further. Multisensors I and II were both used for inhibition analysis of binary paraoxon and carbofuran mixtures in a concentration range 0-5 microg/l, followed by data analysis using feed-forward ANN. The two analytes were determined with prediction errors of 0.4 microg/l for paraoxon and 0.5 microg/l for carbofuran. A complete biosensor assay and subsequent ANN evaluation was completed within 40 min. In addition, multisensor II was also investigated for analyte discrimination in real water samples. Finally, the properties of the multisensors were confirmed by simultaneous detection of binary organophosphate mixtures. Malaoxon and paraoxon in composite solutions of 0-5 microg/l were discriminated with predication errors of 0.9 and 1.6 microg/l, respectively.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","2011","Balbuena, P., Li, W., Ehrich, M.","Assessments of tight junction proteins occludin, claudin 5 and scaffold proteins ZO1 and ZO2 in endothelial cells of the rat blood-brain barrier: Cellular responses to neurotoxicants malathion and lead acetate","","32(1):58-67","10429bff-a1d9-476c-8f87-796dda0a3504","","The blood-brain barrier (BBB) is essential for central nervous system (CNS) normal function. It is formed by endothelial cells with special characteristics, which confer the BBB with low permeability and high transendothelial electrical resistance (TEER). We previously demonstrated that malathion and lead, two neurotoxicants widely present in the environment, decrease TEER and increase permeability in in vitro models of the BBB. In this study we assessed tight junction disruption at the protein and gene expression levels using a rat brain microvascular endothelial cell line (RBE4) exposed to lead acetate at 10-5M and 10-6M, malathion at 10-5M, malaoxon at 10-6M, and their combinations. Cells were incubated with treatments for 2h, 4h, 8h, 16h, and 24h periods. Immunoblotting assessments demonstrated that protein levels of tight junction proteins occludin and claudin 5, and scaffold proteins ZO1 and ZO2 were decreased after treatments. Gene expression determinations did not correlate with the decreases in protein, indicating that the effects on these proteins were post-translational. Â© 2010 Elsevier
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"Unknown","Unknown","Unknown","Unknown","","","2015","Barash, C. I.","Emerging Translational Research Methods: A Sampling","","7:1","4961c722-be01-43c7-9419-92049b6b4fbe","","","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","2011","Barry, K. H., Koutros, S., Berndt, S. I., Andreotti, G., Hoppin, J. A., Sandler, D. P., Burdette, L. A., Yeager, M., Freeman, L. E. B., Lubin, J. H., Ma, X., Zheng, T., Alavanja, M. C. R.","Genetic

variation in base excision repair pathway genes, pesticide exposure, and prostate cancer risk","","119(12):1726-1732","919b3eaa-3f84-451d-a22e-6beedd7d22e3","","Background: Previous research indicates increased prostate cancer risk for pesticide applicators and pesticide manufacturing workers. Although underlying mechanisms are unknown, evidence suggests a role of oxidative DNA damage. Objectives: Because base excision repair (BER) is the predominant pathway involved in repairing oxidative damage, we evaluated interactions between 39 pesticides and 394 tag single-nucleotide polymorphisms (SNPs) for 31 BER genes among 776 prostate cancer cases and 1,444 male controls in a nested case-control study of white Agricultural Health Study (AHS) pesticide applicators. Methods: We used likelihood ratio tests from logistic regression models to determine p-values for interactions between three-level pesticide exposure variables (none/low/high) and SNPs (assuming a dominant model), and the false discovery rate (FDR) multiple comparison adjustment approach. Results: The interaction between fonofos and rs1983132 in NEIL3 [nei endonuclease VIII-like 3 (Escherichia coli)], which encodes a glycosylase that can initiate BER, was the most significant over-all [interaction p-value (pinteract) = 9.3 Ã- 10-6; FDR-adjusted p-value = 0.01]. Fonofos exposure was associated with a monotonic increase in prostate cancer risk among men with CT/TT genot{stroke}ypes for rs1983132 [odds ratios (95% confidence intervals) for low and high use compared with no use were 1.65 (0.91, 3.01) and 3.25 (1.78, 5.92), respectively], whereas fonofos was not associated with prostate cancer risk among men with the CC genot{stroke}ype. Carbofuran and S-ethyl dipropylt{stroke}hiocarbamate (EPTC) interacted similarly with rs1983132; however, these interactions did not meet an FDR < 0.2. Conclusions: Our significant finding regarding fonofos is consistent with previous AHS findings of increased prostate cancer risk with fonofos exposure among those with a family history of prostate cancer. Although requiring replication, our findings suggest a role of BER genetic variation in pesticide-associated prostate cancer risk.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","2013","Basilua Kanza, J. P., El Fahime, E., Alaoui, S., Essassi el, M., Brooke, B., Nkebolo Malafu, A., Watsenga Tezzo, F.","Pyrethroid, DDT and malathion resistance in the malaria vector Anopheles gambiae from the Democratic Republic of Congo","Transactions of the Royal Society of Tropical Medicine and Hygiene","107(1):8-14","eeec34a6-58c7-49a4-9bc2-47de42779a39","","BACKGROUND: Malaria remains the most important parasitic disease in sub-Saharan Africa. We investigated the extent of resistance in the malaria vector Anopheles gambiae from the Democratic Republic of Congo (DRC) to three classes of insecticide approved by WHO for indoor residual spraying. METHOD: Standard WHO bioassays were performed on adult Anopheles mosquitoes reared in the laboratory from larvae collected from different sites. Molecular techniques were used for species identification and to identify knockdown resistance (kdr) and acetylcholinesterase (ace-1(R)) mutations in individual mosquitoes. RESULTS: Only A. gambiae s.s., the nominal member of the A. gambiae species complex, was found. Bioassays showed phenotypic resistance to the main insecticides used in the region, notably pyrethroids (deltamethrin, permethrin, lambda-cyhalothrin), an organochlorine (DDT) and an organophosphate (malathion). The L1014F kdr allele, often associated with resistance to pyrethroids and DDT, was detected in samples from all collection sites at varying frequencies. No ace-1(R) resistance alleles (associated with organophosphate and carbamate resistance) were detected. CONCLUSIONS: These data can be used to inform a resistance management strategy that requires comprehensive information concerning

malaria vector species composition in the areas of interest, and their susceptibility to the insecticides proposed for their
control.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","2011","Baskurt, S., Taskin, B. G., Dogac, E., Taskin, V.","Polymorphism in the acetylcholinesterase gene of Musca domestica L. field populations in Turkey","Journal of vector ecology : journal of the Society for Vector Ecology","36(2):248-57","1a9a4ca1-9f5a-4c97-9a87-4151221ab425","","Acetylcholinesterase (AChE), encoded by the Ace gene, is the primary target of organophosphates (OPs) and carbamates (CBs) in insects. Ace mutations have been identified in OP and CB resistant strains of Musca domestica. In this study, the Ace gene was partially amplified and sequenced at amino acid positions 260, 342, and 407 to determine the frequencies of these mutations in housefly samples collected from farms and garbage disposal sites of 16 provinces in the Aegean and Mediterranean regions of Turkey. In addition, the percent remaining AChE activities in these samples were assayed by using three OPs (malaoxon, paraoxon, and dichlorvos) and one CB (carbaryl) compound as inhibitors. In all the analyzed samples, 13 different combinations at the three amino acid positions were identified and the L/V260-A/G342-F/Y407 combination was found in the highest frequency. No susceptible individual was detected. The highest mean percent remaining AChE activities were detected in the individuals having the L260-A/G342-F/Y407 genotype when malaoxon and paraoxon were used as inhibitors and in the individuals with the L260-A342-F/Y407 combination when dichlorvos and carbaryl were used as inhibitors. The obtained data were heterogeneous and there was no exact correlation between the molecular genetic background and the resistance phenotypes of the flies. The findings of this study at the molecular and biochemical levels indicate the presence of significant control problems in the field.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","2010","Battaglia, C. L. R., Gogal Jr, R. M., Zimmerman, K., Misra, H. P.","Malathion, lindane, and piperonyl butoxide, individually or in combined mixtures, induce immunotoxicity via apoptosis in murine splenocytes in vitro","","29(2):209-220","73de063b-a467-4353-9960-e9565f2edc38","","Lindane, malathion, and piperonyl butoxide were cultured singly or as mixtures with murine splenocytes to evaluate changes in cell death and caused cytotoxicity in a concentration- and time-dependent manner. Pesticide mixture studies were then performed based on minimum cytotoxicity concentrations (<LC25). Cytologic analysis and the alamarBlue assay revealed that individual pesticides and mixtures of malathion/lindane and malathion/piperonyl butoxide prompted cytotoxicity, which was supported by DNA ladder analysis. Using 7-aminoactinomycin D, apoptosis was quantified at 6.5%, 12.0%, 13.2%, 19.3%, and 23.4% for malathion, lindane, piperonyl butoxide, malathion-lindane, and malathion-piperonyl butoxide, respectively. Staining with 7-aminoactinomycin D and B- or T-cell-specific fluorescent-labeled monoclonal antibodies showed B cells to be more susceptible to malathion and piperonyl butoxide treatments than T cells. Treatment of murine splenocytes in vitro with minimum cytotoxic concentrations of lindane, malathion, and piperonyl butoxide and their mixtures induced apoptosis, the effect elicited by the mixtures being additive compared with the individual pesticide effect. Â© The Author(s)
2010.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","2015","Bellai, G. L., Mouhamadou, C. S., Adja, A. M., N'Goran, K. E.","Pyrethroid and DDT resistance in Anopheles gambiae from

Taabo, south-central Cote d'Ivoire","","20:142","b6f693c6-21af-4a38-821a-cdf4c365cb0d","","Malaria prevention can be done by the use of insecticides as Indoor Residual Spraying (IRS) or by the use of Insecticide Treated Nets (ITNs). The development of resistance to insecticides in malaria vectors constitutes a real threat given the emphasis on the use of IRS and ITNs for malaria control. This highlights the importance of assessing the level of resistance to insecticides in vectors before any vector control action. In this context, the resistance level of the major malaria vector, Anopheles.gambiae s.l, was evaluated for the four main families of insecticides used in public health and agriculture (pyrethroids (Deltamethrin 0.05%, permethrin 0.75%), organochlorine (DDT 4%), organophosphate (malathion 5%), carbamate (propoxur 0.1%) in three locations (Taabo-CitÃ©, N'denou, Tokohiri) in the subprefecture of Taabo, CÃ´te d'Ivoire. Susceptibility test were performed according to WHO test cylinders with adult females of An. gambiae aged 2-5 days. The results showed that the three mosquito populations were resistant to DDT (Taabo-CitÃ©: mortality = 17.1%, N'denou: mortality = 5.6%, Tokohiri: mortality = 0%). Mosquitoes from Taabo-CitÃ© and N'denou were resistant to deltamethrin respectively with 89.7% and 85% mortality rates. A probable resistance was suspected with permethrin in these two populations with 97% and 93% of mortality respectively. Contrarily, at Tokohiri, mosquitoes were resistant to permethrin (mortality = 54.4%) and had a decreased sensitivity to deltamethrin (mortality = 91.6%). The molecular forms M and S were identified in overall with the predominance of S form (80.4%). The resistance mechanism involved was the kdr mutation with a frequency of 56.3%. A widespread resistance of wild populations of An.gambiae s.l to DDT and pyrethroids was observed in the three communities, contrarily to the other family of insecticides where the levels of resistance observed varied. Any vector control program in these areas should take into account these observations.","","","RefMan","","","","","","","","","","Unknown","Unknown","Unknown","Unknown","","","2011","Bernhardt, V., D'Souza, J., Shantaram, M.","In vivo genetic damage induced by commercial Malathion and the antigenotoxic role of Withania somnifera","","11(2):78-84","070dafba-48fa-480f-8390-5ff19d590f93","","Commercial grade formulations of Malathion, a commonly used organophosphorus insecticide are reported to contain impurities such as Isomalathion and Malaoxon which increase the toxicity of commercial grade Malathion (CGM). In order to elucidate the genotoxic potency of CGM, its DNA-damaging effect was investigated by use of the comet assay. Trypan blue exclusion test was carried out to evaluate whether CGM causes cytotoxicity of the peripheral lymphocytes. We also evaluated the role of Withania somnifera L (WS) as an antigenotoxic agent that could reduce CGM induced genotoxicity. Therefore, Malathion can be regarded as a potential mutagen and carcinogen due to its DNA damaging effects and WS plays a role in reducing the genotoxic effects and thus can be used as a potent antigenotoxic compound. Our results suggest that Withaniacan be effective in preventing genotoxic effects of CGM. Â© IJIB, All rights reserved.","","","RefMan","","","","","","","","","","Unknown","Unknown","Unknown","Unknown","","","2015","Bhardwaj, J. K., Saraf, P.","Granulosa cell apoptosis by impairing antioxidant defense system and cellular integrity in caprine antral follicles post malathion exposure","","","6e8b064c-edb9-4a0c-be36-1dbf4f432a38","","Toxicological studies have demonstrated the exposure-risk relationship of several pesticides on reproduction of living organisms. To evaluate the role of malathion as a reproductive toxicant, this study aims at assessing the cytological and biochemical changes in the granulosa cells after malathion exposure in

dose (1 nM, 10 nM, 100 nM) and time (4 h, 6 h, 8 h) dependent manner. Histomorphological analysis, fluorescence assay, apoptosis quantification, and terminal deoxynucleotidyl transferase d-UTP mediated nick end labeling (TUNEL) assay were done to determine cytological changes, whereas antioxidant enzyme assays were done to measure the oxidative stress in malathion treated ovarian antral follicles. Histological studies exhibited the occurrence of highly condensed or marginated chromatin with fragmented nucleus, pyknosis, loss of membrane integrity, increased empty spaces, and vacuolization in malathion treated granulosa cells. Ethidium bromide/acridine orange (EB/AO) fluorescence staining demonstrated a significant increase in incidence and percentage of apoptosis after malathion exposure ($p<0.001$), both between and within the groups. Malathion exposure also resulted in increased DNA fragmentation and decline in both antioxidant enzymes activity namely catalase (CAT) and superoxide dismutase (SOD) in granulosa cells of antral follicles. Moreover, there was found a significant negative correlation between the apoptosis incidence and the level of antioxidant enzymes activity, SOD ($r=-0.73$ $p<0.01$) and CAT ($r=-0.80$ $p<0.01$), in malathion treated ovarian antral follicles. Thus, highlighting the role of DNA fragmentation and declining antioxidant level as a possible mechanism underlying malathion induced reproductive toxicity.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","2015","Bianchi, J., Mantovani, M. S., Marin-Morales, M. A.","Analysis of the genotoxic potential of low concentrations of Malathion on the Allium cepa cells and rat hepatoma tissue culture","Journal of environmental sciences (China)","36:102-11","b6a46c1d-c66f-4d0d-966e-6bb137efa09f","","Based on the concentration of Malathion used in the field, we evaluated the genotoxic potential of low concentrations of this insecticide on meristematic and F1 cells of Allium cepa and on rat hepatoma tissue culture (HTC cells). In the A. cepa, chromosomal aberrations (CAs), micronuclei (MN), and mitotic index (MI) were evaluated by exposing the cells at 1.5, 0.75, 0.37, and 0.18mg/mL of Malathion for 24 and 48hr of exposure and 48hr of recovery time. The results showed that all concentrations were genotoxic to A. cepa cells. However, the analysis of the MI has showed non-relevant effects. Chromosomal bridges were the CA more frequently induced, indicating the clastogenic action of Malathion. After the recovery period, the higher concentrations continued to induce genotoxic effects, unlike the observed for the lowest concentrations tested. In HTC cells, the genotoxicity of Malathion was evaluated by the MN test and the comet assay by exposing the cells at 0.09, 0.009, and 0.0009mg/5mL culture medium, for 24hr of exposure. In the comet assay, all the concentrations induced genotoxicity in the HTC cells. In the MN test, no significant induction of MN was observed. The genotoxicity induced by the low concentrations of Malathion presented in this work highlights the importance of studying the effects of low concentrations of this pesticide and demonstrates the efficiency of these two test systems for the detection of genetic damage promoted by Malathion.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","2012","Bigoga, J. D., Ndangoh, D. N., Awono-Ambene, P. H., Patchoke, S., Fondjo, E., Leke, R. G.","Pyrethroid resistance in Anopheles gambiae from the rubber cultivated area of Niete, South Region of Cameroon","Acta tropica","124(3):210-4","28f6406f-1f4c-4fa0-862e-2be734631e56","","Anti-vector intervention remains the most effective way of controlling malaria. Although in Cameroon and elsewhere focus is on the use of long-lasting insecticidal nets and indoor residual spraying, the efficacy of both methods

greatly depends on the continuing susceptibility of the vectors to the insecticides used. The emergence and spread of insecticide resistance in the major malaria vectors constitute a huge challenge to control programmes. Consequently, routine monitoring and evaluation of vector resistance status to insecticides are mandatory for early detection of resistance should it arise, and effectively planning future anti-vector interventions especially in areas reputed for routine application in agriculture. The WHO bioassay kit was used to determine the susceptibility status of Anopheles gambiae s.l. populations to seven insecticides belonging to four classes (organochlorine, organophosphate, carbamate and pyrethroids) in Niete, an area of intense rubber cultivation in southern forested Cameroon. Species and molecular forms of An. gambiae s.l. as well as the presence of knock down resistance (kdr) mutations were determined using polymerase chain reaction (PCR) techniques. All Anopheles tested was identified as An. gambiae s.s. and of the M molecular form. Based on WHO classification, while the mosquitoes were fully (100%) susceptible to malathion and bendiocarb, resistance was confirmed to DDT and the pyrethroids, permethrin and lambda-cyhalothrin. The other pyrethroids (deltamethrin and cyfluthrin) showed signs of developing resistance. Resistance to DDT and pyrethroids is indicative of existing cross resistance mechanisms between these insecticides. The increase in knockdown times was greater than twofold that of the reference susceptible strain, suggesting the possible involvement of kdr mutations, also confirmed in this study. The findings highlight the need for constant evaluation, re-evaluation and monitoring of the insecticides for malaria vector control in Cameroon. However, bendiocarb and malathion can be used and may require alternation or combination with insecticides of other classes to better manage the occurrence and spread of resistance in Niete.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","1999","Blasiak, J., Jaloszynski, P., Trzeciak, A., Szyfter, K.","In vitro studies on the genotoxicity of the organophosphorus insecticide malathion and its two analogues","Mutation research","445(2):275-83","c0236203-de60-4cd4-9f15-09908d88d038","","Malathion [S-(1,2-dicarboethoxyethyl)O,O-dimethyl phosphorodithioate] is a commonly used organophosphorus insecticide reported to be genotoxic both in vivo and in vitro, but the reports are conflicting. In order to elucidate the genotoxic potency of the main compounds present in commercial preparations of malathion, the DNA-damaging effect of this insecticide, its major metabolite malaoxon [S-(1,2-dicarboethoxyethyl)O,O-dimethyl phosphorothiolate] and its isomer isomalathion [S-(1,2-dicarboethoxyethyl)O,S-dimethyl phosphorodithioate], all at purity of at least 99.8%, was investigated by use of the alkaline single cell gel electrophoresis (comet assay). Freshly isolated human peripheral blood lymphocytes were incubated with 25, 75 and 200 microM of the chemicals for 1 h at 37 degrees C. The concentrations used are comparable to those found in blood following various non-lethal human exposures to pesticides. Malathion did not cause any significant changes in the comet length of the lymphocytes, throughout the range of concentrations tested. Malaoxon and isomalathion introduced damage to DNA in a dose-dependent manner. The effect induced by malaoxon was more pronounced than that caused by isomalathion. Treated cells were able to recover within a 60-min incubation in insecticide-free medium at 37 degrees C except the lymphocytes exposed to malaoxon at 200 microM, which did not show measurable DNA repair. The latter result suggests a considerable cytotoxic effect (cell death) of malaoxon at the highest concentration used. The reported genotoxicity of malathion might, therefore, be a consequence of its metabolic biotransformation to malaoxon or the presence of malaoxon and/or isomalathion

as well as other unspecified impurities in commercial formulations of malathion. In this regard, the results of our study clearly indicate that malathion used as commercial product, i.e., containing malaoxon and isomalathion, can be considered as a genotoxic substance in vitro. This means that it may also produce DNA disturbances in vivo, such as DNA breakage at sites of oncogenes or tumor suppressor genes, thus playing a role in the induction of malignancies in individuals exposed to this agent. Therefore, malathion can be regarded as a potential mutagen/carcinogen and requires further investigation.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","2012","Bouvresse, S., Berdjane, Z., Durand, R., Bouscaillou, J., Izri, A., Chosidow, O.","Permethrin and malathion resistance in head lice: results of ex vivo and molecular assays","Journal of the American Academy of Dermatology","67(6):1143-50","129a2e1b-07b3-4ff9-ae52-950d1e81d268","","BACKGROUND: Treatment of head lice infestation relies on the application of topical insecticides. Overuse of these products has led to the emergence of resistance to pyrethroids and malathion worldwide. Permethrin resistance in head lice is mostly conferred by the knockdown resistance (kdr) trait. OBJECTIVE: To evaluate the occurrence of permethrin- and malathion-resistant head lice in Paris. METHODS: A prospective survey was conducted in 74 elementary schools. Live lice collected on schoolchildren were randomly selected and submitted to ex vivo bioassays or underwent individual DNA extraction. A fragment of kdr-like gene was amplified and compared with wild-type sequences. RESULTS: Live head lice were detected in 574 children. Ex vivo assays showed no surviving lice after a 1-hour contact with malathion while most lice died after a 1-hour exposure to permethrin and piperonyl butoxide (85.7%, 95% confidence interval [CI]: 83.9-87.5). Among the 670 lice with workable DNA sequences, 661 lice (98.7%, 95% CI 97.7-99.3) had homozygous kdr mutations. LIMITATIONS: The findings of this large-scale survey of the occurrence of insecticide-resistant head lice indicated a major insecticide pressure in the study population, but it was not sufficient to draw conclusions about other populations. The presence of T917I-L920F mutations in kdr gene may not correlate with treatment failure in prospective studies. CONCLUSION: The high occurrence of kdr mutant allele suggests that insecticide resistance was already strongly established in the studied population. This finding must be interpreted with caution as it may not be predictive of treatment failure.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","2009","Buchanan, I., Liang, H. C., Khan, W., Liu, Z., Singh, R., Ikehata, K., Chelme-Ayala, P.","Pesticides and herbicides","","81(10):1731-1816","920701b0-ac9e-4395-b277-d8d2ba7eca8d","","This is a review of literature published in 2008 that covered issues related to the presence of pesticides and herbicides in the environment. The review is divided into nine sections, including analytical methods, toxicology, monitoring, ecology, fate and transport, modeling, risk assessment, management and minimization, as well as treatment strategies. Copyright Â© 2009 Water Environment Federation.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","2010","Buchanan, I., Liang, H. C., Liu, Z., Razaviarani, V., Rahman, Md Z.","Pesticides and herbicides","","82(10):1594-1693","d13605b2-888c-4441-bdb1-62590d718e66","","This is a review of literature published in 2009 that covered issues related to the presence of pesticides and herbicides in the environment. The review is divided into nine sections, including analytical methods, toxicology, monitoring, ecology, fate and transport, modeling, risk

assessment, management and minimization, and treatment strategies. Copyright Â© 2010 Water Environment Federation.","","","RefMan","","","","","","","","","" "Unknown","Unknown","Unknown","Unknown","","","2010","Calaf, G. M., Balajee, A. S., Roy, D.","Molecular markers for breast carcinogenesis models induced by environmental substances and estrogen","","70(8)","a024fc93-78d9-4388-ae35-b37a9a80b804","","Breast cancer is the most common cancer in women throughout the world. Exogenous and endogenous agents such as environmental carcinogens and female hormones seem to be involved in the etiology of breast cancer. It is a multistage process involving a series of genetic alterations, identification of potential genes responsible for breast carcinogenesis is critical for timely diagnosis and prevention of breast cancer. To gain insights into the mechanisms for breast cancer initiation and development processes by exogenous environmental agents, we have developed many experimental breast cancer model systems: In vitro model with the immortalized human breast epithelial cell line, MCF-10F exposed to (I) low doses of high LET (linear energy transfer) alpha particles (150 keV/Î¼m) (Carcinogenesis 21: 769, 2000) and b), (II) organophosphorous pesticides, either with Parathion (P) or Malathion (M) and (III) combination of either P or M in the presence of estrogen (E). Results showed that MCF-10F cells treated either with double dose of 60 cGy alpha particles in the presence of E or pesticides induced malignant transformation of MCF-10F. The malignant transformation was determined by multiple biological assays: increased cell proliferation, anchorage independency, invasive capabilities and tumor formation in nude mice, microsatellite instability and loss of heterozygosity in chromosomes 17, 11, 6, 8. Gene expression analysis using cancer pathway specific and affymetrix arrays detected alterations in the expression levels of p53, ErbB2, BRCA1, c-Ha-ras, Rho-A, PTEN, RB, c-Ha-ras, transforming protein Rho-A, F, GDP, TGF alpha, beta receptor, integrin B6, Notch3 and cathepsin. In addition to the in vitro human model, in vivo rat mammary gland model was also generated: (I) control (II) either P or M (III) E and (IV) P or M and E. Animals were treated for 5 days. These combined treatments induced significant progressive morphological and molecular changes. Alterations in the expression levels of RNA and protein were observed for c-fos, c-myc, mutant p53, ErbB2, BRCA1, c-Ha-ras, Rho-A, CYP1A1 gene and protein expression in the rat mammary gland after 240 days of treatment in comparison to control. Such stimulation led to mammary tumor formation. Collectively, our study shows the molecular signature of oncogenic deregulation in breast cancer progression induced by the combination of environmental substances and estrogen. Thus, aberrant expression of multiple genes involved in key signaling pathways renders these models as important tools for monitoring carcinogenic progression and chemo-intervention.","","","RefMan","","","","","","","","","" "Unknown","Unknown","Unknown","Unknown","","","2009","Calaf, G. M., Echiburu-Chau, C., Roy, D.","Organophosphorous pesticides and estrogen induce transformation of breast cells affecting p53 and c-Ha-ras genes","International journal of oncology","35(5):1061-8","e485e792-f0b2-4e98-8715-dea59e2505cc","","Cancer progression has been associated with an increase in genomic instability indicated by inactivation of tumor suppressor genes and activation of oncogenes. Epidemiological and experimental evidence has implicated estrogens in the etiology of breast cancer. To study environmental organophosphorous pesticides is of interest since evidence indicate that pesticides may enhance cell division, increasing the risk of breast cancer. The aim was to evaluate the effects of these pesticides, such as parathion and malathion in the presence of estrogen on malignant transformation as well as on genomic instability,

that is in the frequency of loss of heterozygosity (LOH) and microsatellite instability (MSI). The MCF-10F immortalized human breast epithelial cell line, that was treated with parathion or malathion alone and in combination with estrogen was used. These studies indicated that either pesticide alone or in combination with estrogen induced malignant transformation as shown by anchorage-independent growth capability and invasive characteristics in comparison to control. Such malignant phenotypic characteristics were corroborated by significant (P<0.05) increase in p53 and c-Ha-ras protein expression. Results indicated different degrees of allelic imbalance in the form of LOH or MSI with different microsatellite markers. MSI was found in malathion and estrogen-treated cells with a marker used for p53 tumor suppressor gene at loci 17p13.1. The same combination of substances presented MSI with a marker used for c-Ha-ras mapped in chromosome 11p14.1, as well as mutations in c-Ha-ras for codons 12 and 61. LOH was observed in codon 12 in the presence of estrogen or malathion alone. Parathion alone and combined with estrogen induced MSI in codon 61. It can be concluded that the organophosphorous pesticides parathion and malathion induced malignant transformation of breast cells through genomic instability altering p53 and c-Ha-ras, considered pivotal to cancer process.","","","RefMan","","","","","","","","","" "Unknown","Unknown","Unknown","Unknown","","","1997","Campbell, P. M., Trott, J. F., Claudianos, C., Smyth, K. A., Russell, R. J., Oakeshott, J. G.","Biochemistry of esterases associated with organophosphate resistance in Lucilia cuprina with comparisons to putative orthologues in other Diptera","Biochemical genetics","35(1-2):17-40","f34fef37-c9fd-45f5-9f18-5d7c2a4908ed","","Esterase activities associated with organophosphate insecticide resistance in the Australian sheep blowfly, Lucilia cuprina, are compared with similar activities in other Diptera. The enzymes making the major contribution to methyl butyrate hydrolysis (""ali-esterase"") in L. cuprina, M. domestica, and D. melanogaster comigrate during electrophoresis. The enzymes in L. cuprina and D. melanogaster correspond to the naphthyl acetate hydrolyzing E3 and EST23 isozymes of those species. These and previously published data suggest that the ali-esterases of all three species are orthologous. Strains of L. cuprina fall into four groups on the basis of quantitative determinations of their ali-estesterase, OP hydrolase, and malathion carboxylesterase activities and these groups correspond to their status with respect to two types of OP resistance. Strains susceptible to OP's have high ali-esterase, low OP hydrolase, and intermediate MCE activities; those resistant to malathion but not diazinon have low ali-esterase, intermediate OP hydrolase, and high MCE activities; those resistant to diazinon but not malathion have low ali-esterase, high OP hydrolase, and low MCE activities; those resistant to both OPs have low ali-esterase, high OP hydrolase, and high MCE activities. The correlated changes among the three biochemical and two resistance phenotypes suggest that they are all properties of one gene/enzyme system; three major allelic variants of that system explain OP susceptibility and the two types of OP resistance. Models are proposed to explain the joint contribution of OP hydrolase and MCE activities to malathion resistance and the invariant association of low ali-esterase and elevated OP hydrolase activities in either type of resistance.","","","RefMan","","","","","","","","","" "Unknown","Unknown","Unknown","Unknown","","","2011","Chanda, E., Musapa, M., Hemingway, J., Shinondo, C. J., Seyoum, A., Mumba, P., Kamuliwo, M., Coleman, M.","Insecticide resistance management: The key to continued success of malaria vector control in Zambia","","85(6):134","112eeee2c-7d7d-4a5a-bec8-d8b1f1b885a0","","In the absence of a vaccine, insecticide-based vector control has been harnessed for

prevention of malaria transmission in endemic countries. In Zambia indoor residual spraying (IRS) with DDT (2g/m2) and pyrethroids (25mg/m2) and insecticide treated nets (ITNs) are implemented as frontline interventions. However, their continued effcacy for successful and sustainable malaria vector control is threatened by emergence of resistance in Anopheles species in Africa. Studies to evaluate the spatiotemporal resistance profles in malaria vectors were conducted in spatially segregated localities. A total of 4,581 F1 generation An. gambiae s,l (2,745) and An. funestus (1,836) were assayed for susceptibility using WHO standard discriminating dosages. Both Leu-Phe (west) and Leu-Ser (east) knock down resistance (kdr) mutations assays were investigated. By 2004, no resistance had been detected in either An. gambiae s.l. or An. funestus in Zambia. Between 2009 and 2011 signifcant levels of resistance to pyrethroids (0.05% deltamethrin, 0.05% lambda-cyhalothrin and 0.75% permethrin) and DDT (4%) were detected in both species ($p < 0.001$). High levels of Leu-Phe (west) kdr mutation and monooxygenases (P450) have been detected in An. gambiae s.s and An. funestus respectively. Marked levels of resistance were detected in IRS than in ITNs areas. No resistance was detected to the carbamate (0.01% bendiocarb) or the organophosphate (5% malathion) in either species. This implies that resistance selection is due to scaled up IRS and ITNs and could potentially undermine malaria control. This has resulted in a change of IRS policy from pyrethroids and DDT to carbamates. To preserve the limited arsenal of insecticides, good stewardship through a rational insecticide resistance management strategy is critical. Thus a strong partnership has been set up and data on potential underlying mechanisms of insecticide resistance, factors contributing to its emergence and distribution is being collated. This will ensure evidence-based choice of insecticides and their prolonged effcacy in Zambia.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","2014","Chang, X., Zhong, D., Fang, Q., Hartsel, J., Zhou, G., Shi, L., Fang, F., Zhu, C., Yan, G.","Multiple Resistances and Complex Mechanisms of Anopheles sinensis Mosquito: A Major Obstacle to Mosquito-Borne Diseases Control and Elimination in China","","8(5)","8fbdce9c-b98b-4b9b-9618-91bf7825b3a0","","Malaria, dengue fever, and filariasis are three of the most common mosquito-borne diseases worldwide. Malaria and lymphatic filariasis can occur as concomitant human infections while also sharing common mosquito vectors. The overall prevalence and health significance of malaria and filariasis have made them top priorities for global elimination and control programmes. Pyrethroid resistance in anopheline mosquito vectors represents a highly significant problem to malaria control worldwide. Several methods have been proposed to mitigate insecticide resistance, including rotational use of insecticides with different modes of action. Anopheles sinensis, an important malaria and filariasis vector in Southeast Asia, represents an interesting mosquito species for examining the consequences of long-term insecticide rotation use on resistance. We examined insecticide resistance in two An. Sinensis populations from central and southern China against pyrethroids, organochlorines, organophosphates, and carbamates, which are the major classes of insecticides recommended for indoor residual spray. We found that the mosquito populations were highly resistant to the four classes of insecticides. High frequency of kdr mutation was revealed in the central population, whereas no kdr mutation was detected in the southern population. The frequency of G119S mutation in the ace-1 gene was moderate in both populations. The classification and regression trees (CART) statistical analysis found that metabolic detoxification was the most important resistance mechanism,

whereas target site insensitivity of L1014 kdr mutation played a less important role. Our results indicate that metabolic detoxification was the dominant mechanism of resistance compared to target site insensitivity, and suggests that long-term rotational use of various insecticides has led An. sinensis to evolve a high insecticide resistance. This study highlights the complex network of mechanisms conferring multiple resistances to chemical insecticides in mosquito vectors and it has important implication for designing and implementing vector resistance management strategies. Â© 2014 Chang et al.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","2015","Charalampous, N., Kindou, A., Vlastos, D., Tsarpali, V., Antonopoulou, M., Konstantinou, I., Dailianis, S.","A Multidisciplinary Assessment of River Surface Water Quality in Areas Heavily Influenced by Human Activities","Archives of environmental contamination and toxicology","69(2):208-22","4fd455a2-3452-4a19-a5a9-de265a683895","","The present study could serve as a multidisciplinary approach for the assessment of river surface water quality with the use of chemical and biological methods. Specifically, physicochemical parameters, heavy metals, and pesticides were measured in water samples from three different stations (sampling station S1, S2, and S3) along Asopos River (Greece). In parallel, algal species (primary producers)-such as Scenedesmus rubescens and Chlorococcum sp.; consumer invertebrate species, such as the fairy shrimp Thamnocephalus platyurus and the rotifer Brachionus calyciflorus; as well as human lymphocytes-were exposed to those samples for assessing their toxic and genotoxic/mutagenic effects. According to the results, although the values of almost all of the physicochemical parameters tested, heavy metals (zinc, cadmium, lead, and mercury) and pesticides were lower than or within the respective environmental quality standards, thus offering no clear evidence for their natural or anthropogenic origin. Values recorded for nickel, chromium, hexavalent chromium, and malathion represent a typical case of mixed influence from natural and anthropogenic enrichments. In contrast, the algal growth arrest, the acute toxic effects on the freshwater invertebrates, and the increased micronuclei frequencies observed in human lymphocytes showed the presence of human-derived hazardous substances, which were hardly determinable with the use of conventional chemical methods. Given that the presence of priority pollutants in river surface waters, heavily burdened by anthropogenic activities, could give no clear evidence for their biological risk, the results of the present study showed that chemical and biological assays should be applied in parallel, thus serving as a reliable tool for the assessment of river water quality.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","2006","Chen, X. Y., Shao, J. Z., Xiang, L. X., Liu, X. M.","Involvement of apoptosis in malathion-induced cytotoxicity in a grass carp (Ctenopharyngodon idellus) cell line","Comparative biochemistry and physiology. Toxicology & pharmacology : CBP","142(1-2):36-45","c48b2cb7-a45a-4536-8897-7bac070c45f9","","We investigated the role of apoptosis in malathion-induced cytotoxicity in the grass carp (Ctenopharyngodon idellus) cell line ZC-7901. Fish cells were treated with different concentrations of malathion (0.62-95 mg/L), and the IC(50) ranged from 37.94+/-1.93 mg/L for 12 h to 3.04+/-0.27 mg/L for 72 h by the MTT assay. Apoptosis was detected by confocal laser scanning microscopy, transmission electron microscopy, TUNEL reaction, DNA laddering and a flow cytometric PI staining assay. The results demonstrated that apoptosis was involved in the cytotoxic effect of malathion, and that malathion-induced apoptosis occurred in a dose- and time-dependent manner. In

addition, the induction of apoptosis by malathion was accompanied by mitochondrial membrane potential (DeltaPsi(m)) disruption, intracellular Ca(2+) elevation, generation of reactive oxygen species (ROS) and ATP depletion. Our investigation suggested that malathion exerts its cytotoxic effects by the induction of apoptosis via a direct effect on the mitochondria.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","2002","Clemedson, C., Nordin-Andersson, M., Bjerregaard, H. F., Clausen, J., Forsby, A., Gustafsson, H., Hansson, U., Isomaa, B., Jorgensen, C., Kolman, A., Kotova, N., Krause, G., Kristen, U., Kurppa, K., Romert, L., Scheers, E.","Development of an in vitro test battery for the estimation of acute human systemic toxicity: An outline of the EDIT project. Evaluation-guided Development of New In Vitro Test Batteries","Alternatives to laboratory animals : ATLA","30(3):313-21","a6c9ead1-1c1b-4b74-a2f0-6182ba6be182","","The aim of the Evaluation-guided Development of new In Vitro Test Batteries (EDIT) multicentre programme is to establish and validate in vitro tests relevant to toxicokinetics and for organ-specific toxicity, to be incorporated into optimal test batteries for the estimation of human acute systemic toxicity. The scientific basis of EDIT is the good prediction of human acute toxicity obtained with three human cell line tests (R(2) = 0.77), in the Multicentre Evaluation of In Vitro Cytotoxicity (MEIC) programme. However, the results from the MEIC study indicated that at least two other types of in vitro test ought to be added to the existing test battery to improve the prediction of human acute systemic toxicity - to determine key kinetic events (such as biotransformation and passage through biological barriers), and to predict crucial organ-specific mechanisms not covered by the tests in the MEIC battery. The EDIT programme will be a case-by-case project, but the establishment and validation of new tests will be carried through by a common, step-wise procedure. The Scientific Committee of the EDIT programme defines the need for a specific set of toxicity or toxicokinetic data. Laboratories are then invited to perform the defined tests in order to provide the ""missing"" data for the EDIT reference chemicals. The results obtained will be evaluated against the MEMO (the MEIC Monograph programme) database, i.e. against human acute systemic lethal and toxicity data. The aim of the round-table discussions at the 19th Scandinavian Society for Cell Toxicology (SSCT) workshop, held in Ringsted, Denmark on 6-9 September 2001, was to identify which tests are the most important for inclusion in the MEIC battery, i.e. which types of tests the EDIT programme should focus on. It was proposed that it is important to include in vitro methods for various kinetic events, such as biotransformation, absorption in the gut, passage across the blood-brain barrier, distribution volumes, protein binding, and renal clearance/accumulation. Models for target organ toxicity were also discussed. Because several of the outlier chemicals (paracetamol, digoxin, malathion, nicotine, paraquat, atropine and potassium cyanide) in the MEIC in vivo-in vitro evaluation have a neurotoxic potential, it was proposed that the development within the EDIT target organ programme should initially be focused on the nervous system.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","2007","Clere, N., Faure, S.","After the opening of classes, it comes the lice","","(468):25-26","c35ee2ae-615c-489b-a29f-c3502d74ad54","","","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","2012","Coleman, M., Chanda, E., Mulenga, M., Hemingway, J., Strode, C.","An example from zambia of using novel approaches to monitoring and manage insecticide resistance for effective vector control","","87(5):420","c23e78c2-b369-4d3e-8eab-4e5fb901f020","","Increased coverage

with insecticide treated nets (ITNs) and indoor residual spraying (IRS) with DDT and pyrethroids, have led to impressive decreases in malaria transmission in Zambia. However, the detection of high levels of insecticide resistance in both Anopheles gambiae and An. funestus is a serious risk to vector control efforts. In 2011 an Insecticide Resistance Management Technical Working Group was established to develop a plan to sustain current control levels and conserve insecticides for malaria control in the country. Here we report on results from bioassays and molecular analysis of resistance mechanisms for two regions, the Copperbelt and Eastern Provinces of Zambia. A high prevalence of resistance to deltamethrin (27% Mortality), permethrin (34%M), etofenprox (5%M) and DDT (6%M) was detected in An. gambiae from the Copperbelt; the same populations were susceptible to bendiocarb and malathion. Resistance to the pyrethroids and DDT was due to kdr (the 1014F mutation is fixed in this population) and over expression of several p450's including CYP6Z3 and CYP6M3. An. funestus from Eastern Province also exhibited resistance to diagnostic doses of deltamethrin (45% M), permethrin (81.5% M), etofenprox (18%M) and bendiocarb (77% M), but was susceptible to DDT. This population has elevated CYP6P9a, CYP6Z1 and CYP6M3. A more susceptible population of An.funestus was found in the Copperbelt and only had elevated CYP6M3. As well as a different resistance profile in these regions the collections indicated very different malaria vector species abundance patterns that will impact vector control decisions. The impact of this information has allowed the Zambian malaria control programme to move away from ineffective insecticides used in the Copperbelt (DDT) and Eastern (etofenprox) to effective insecticides and to put an insecticide resistance management programme in place with the aim of prolonging the successes already gained. We examine the entomological M & E in Zambia and how lessons learnt here can be applied to other vector control programmes in the
region.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","2007","Corbel, V., N'Guessan, R., Brengues, C., Chandre, F., Djogbenou, L., Martin, T., AkogbÃ©to, M., Hougard, J. M., Rowland, M.","Multiple insecticide resistance mechanisms in Anopheles gambiae and Culex quinquefasciatus from Benin, West Africa","","101(3):207-216","667e1779-3363-4c64-b03b-918129d950c3","","Because free-insecticide treated net distribution is planned in Benin (West Africa) during the next few years, we investigated the type, frequency and distribution of insecticide resistance mechanisms in Anopheles gambiae and Culex quinquefasciatus mosquitoes in four localities selected on the basis of contrasting agricultural practices, use of insecticides and environment. Bioassays with WHO diagnostic test kits were carried out using pyrethroid, carbamate, organophosphate and organochlorine insecticides. An. gambiae mosquitoes were identified to species and to M or S molecular forms using PCR techniques. Molecular and biochemical assays were carried out to identify kdr and Ace.1 mutations in individual mosquitoes and to detect any increase in the activity of enzymes typically involved in insecticide metabolism (oxidase, esterase and glutathion-S-transfÃ©rases). WHO diagnostic tests showed high frequency of resistance in An. gambiae and Cx. quinquefasciatus to permethrin and DDT in three areas. This was consistent with the presence of target site insensitivity due to kdr mutation and to increased metabolism through enzymatic activity. Kdr was expressed in both M and S forms. However, less than 1% of An. gambiae or Cx. quiqnuefasciatus showed the presence of the Ace.1R mutation. Carbamate/OP resistance was present at higher frequency in Culex than in An. gambiae. Dieldrin resistance was present in both species at all four localities. A higher frequency of pyrethroid-

resistance was found in An. gambiae mosquitoes collected in urban areas compared to those collected in rice growing areas. The expansion of vegetable growing within urban areas probably contributed to selection pressure on mosquitoes. The detection of multiple resistance mechanisms in both An. gambiae and Cx. quinquefasciatus in Benin may represent a threat for the efficacy of ITNs and other forms of vector control such as indoor residual spraying in the future. Â© 2007 Elsevier B.V. All rights reserved.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","2010","Cuamba, N., Morgan, J. C., Irving, H., Steven, A., Wondji, C. S.","High level of pyrethroid resistance in an Anopheles funestus population of the Chokwe District in Mozambique","PloS one","5(6):e11010","b748dfa3-2726-4d75-a0b1-8c36e3cb6683","","BACKGROUND: Although Anopheles funestus is difficult to rear, it is crucial to analyse field populations of this malaria vector in order to successfully characterise mechanisms of insecticide resistance observed in this species in Africa. In this study we carried out a large-scale field collection and rearing of An. funestus from Mozambique in order to analyse its susceptibility status to insecticides and to broadly characterise the main resistance mechanisms involved in natural populations. METHODOLOGY/PRINCIPAL FINDINGS: 3,000 F(1) adults were obtained through larval rearing. WHO susceptibility assays indicated a very high resistance to pyrethroids with no mortality recorded after 1 h 30 min exposure and less than 50% mortality at 3 h 30 min. Resistance to the carbamate, bendiocarb was also noted, with 70% mortality after 1h exposure. In contrast, no DDT resistance was observed, indicating that no kdr-type resistance was involved. The sequencing of the acetylcholinesterase gene indicated the absence of the G119S and F455W mutations associated with carbamate and organophosphate resistance. This could explain the absence of malathion resistance in this population. Both biochemical assays and quantitative PCR implicated up-regulated P450 genes in pyrethroid resistance, with GSTs playing a secondary role. The carbamate resistance observed in this population is probably conferred by the observed altered AChE with esterases also involved. CONCLUSION/SIGNIFICANCE: The high level of pyrethroid resistance in this population despite the cessation of pyrethroid use for IRS in 1999 is a serious concern for resistance management strategies such as rotational use of insecticides. As DDT has now been re-introduced for IRS, susceptibility to DDT needs to be closely monitored to prevent the appearance and spread of resistance to this insecticide.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","2007","Cui, F., Qu, H., Cong, J., Liu, X. L., Qiao, C. L.","Do mosquitoes acquire organophosphate resistance by functional changes in carboxylesterases?","FASEB journal : official publication of the Federation of American Societies for Experimental Biology","21(13):3584-91","fe5cee23-8151-4772-8569-083fc06b5220","","Carboxylesterase-based metabolic resistance to organophosphates (OPs) in insects has been shown to originate either from mutations in esterase-encoding sequences or from amplification of esterase genes. This study aimed to test the hypothesis that mosquitoes can acquire OP resistance by functional changes in carboxylesterases. Mutations were introduced into the esterase B1 of mosquito Culex pipiens by site-directed mutagenesis at positions 110 and 224. Three single mutants (G110D, W224L, and W224S) and two double mutants (G110D/W224L and G110D/W224S) were expressed and purified. All five mutants lost native carboxylesterase activity. Mutation W224L converted esterase B1 to an OP hydrolase and increased its malathion carboxylesterase activity. No obvious OP hydrolysis was observed by G110D or W224S. Our

data strongly support our hypothesis and suggest that mutation W224L might occur in natural populations of mosquitoes. Sequence comparison shows that the site 224 is especially highly conserved among various insect carboxylesterases. This leads to another hypothesis: that the position 224 plays a key role in insect carboxylesterases' switching from their native physiological functions to other functional niches under selection pressure exerted by insecticides.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","2006","Cui, F., Raymond, M., Berthomieu, A., Alout, H., Weill, M., Qiao, C. L.","Recent emergence of insensitive acetylcholinesterase in Chinese populations of the mosquito Culex pipiens (Diptera: Culicidae)","Journal of medical entomology","43(5):878-83","2b2b4337-abf6-4dea-8f78-9a950b3a890c","","Organophosphate/carbamate target resistance has emerged in Culex pipiens L. (Diptera: Culicidae), the vector of Wuchereria bancrofti and West Nile virus (family Flaviviridae, genus Flavivirus) in China. The insensitive acetylcholinesterase was detected in only one of 20 samples collected on a north-to-south transect. According to previous findings, a unique mutation, G119S in the ace-1 gene, explained this high insensitivity. Phylogenetic analysis indicates that the mutation G119S recently detected in China results from an independent mutation event. The G119S mutation thus occurred at least three times independently within the Cx. pipiens complex, once in the temperate (Cx. p. pipiens) and twice in the tropical form (Cx. p. quinquefasciatus). Bioassays performed with a purified G119S strain indicated that this substitution was associated with high levels of resistance to chlorpyrifos, fenitrothion, malathion, and parathion, but low levels of resistance to dichlorvos, trichlorfon, and fenthion. Hence, it is possible that in China, dichlorvos, trichlorfon, and fenthion will still achieve effective control even in the presence of the G119S mutation.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","2012","D'Agostino, J., Zhang, H., Kenaan, C., Hollenberg, P.","Mechanism-based inactivation of human cytochrome P450 2B6 by chlorpyrifos and related organophosphate pesticides","","44:33","5860d8cf-52f0-457b-a0b4-3c3c7713ce11","","Chlorpyrifos (CPS) is a commonly used organophosphate pesticide which is bioactivated by P450s to give the toxic metabolite chlorpyrifos-oxon (CPO). This reaction also results in the release of sulfur, which is implicated in mechanismbased inactivation (MBI) of P450s. CYP2B6 was determined to have the greatest catalytic efficiency for CPO formation in vitro, therefore we set out to characterize the MBI of CYP2B6 by CPS. CPS inactivated CYP2B6 in a time- and concentration-dependent manner with a kinact of 1.97 min-1, a Ki of 0.47 Î¼M, and a partition ratio of 17.7. The rate of CPO formation and the rate of the first electron transfer from cytochrome P450 reductase to CYP2B6 in the presence of CPS were determined and the values were supportive of the rapid inactivation observed. We further evaluated the ability of the organophosphate pesticides chlorpyrifos-methyl, diazinon, parathion-methyl, malathion, and azinophos-methyl to inactivate CYP2B6. These organophosphate pesticides were also potent MBIs of CYP2B6 characterized by similar kinact and ki values. The inactivation of CYP2B6 by CPS was accompanied by loss of P450 detectable by its CO reduced spectra and, to a lesser extent, loss of detectable heme. High molecular weight adducts were observed when inactivated CYP2B6 was run on SDS-PAGE gels indicating protein aggregation. We further explored the ability of CPS to inactivate CYP2B1 and CYP2B4, as well as CYP2B6 with mutation of the cysteines at positions 152 or 475 to serine. The results of IC50 shift experiments revealed that only CYP2B6 was inactivated and the inactivation was unaffected by mutation of cysteine to serine at

positions 152 and 475. These results indicate that CPS and other organophosphate pesticides are potent MBIs of CYP2B6, which may have implications in the toxicity of these pesticides as well as potential pesticide-drug interactions.","","","RefMan","","","","","","","","","" "Unknown","Unknown","Unknown","Unknown","","","2012","Darwish, R., Sherif, N., Hassan, M., Mahrous, H.","Chromosomal aberrations as biomarker of exposure to malathion in agriculture workers","","211:S22","f8910e36-47d9-4bc5-917a-ff8b49568e30","","Purpose: In the present study, an attempt has been made to evaluate the genotoxic risk associated with occupational exposure to malathion (a widely used organophosphate pesticide in Egypt) using chromosomal aberrations in circulating lymphocytes of exposed workers as a biological marker of genotoxicity. Methods: The exposed group was composed of 30 male agricultural workers regularly exposed to malathion during spraying. The chromosomal aberration analysis was carried out on cultures of phytohemaglutinin-stimulated blood lymphocytes. 0.5 ml of whole blood was added to 5ml of RPMI-1640 medium supplemented with 1ml serum. Lymphocytes were incubated at 37 Â°C for 48 h. Then colcemid was added at final concentration at 0.2-g/ml for the last 2 h. Fixation and preparation of the slides were carried out according to conventional methods. Results and conclusion: The group of agricultural workers showed a significant increase in the frequency of chromosomal aberrations, mainly of chromatid type (gaps, t = 5.6; and breaks, t = 3.5), when compared to the unexposed control group. A significant correlation was found between the yield of aberrations and the duration of exposure to malathion (r = 0.16, p = 0.01). Our results showed that malathion exhibits a certain mutagenic effect on the genetic structures of the somatic cells of the exposed group. The established positive correlation between the frequency of chromosome aberrations and the duration of exposure suggests the sensitivity of cytogenetic analyses in the detection of a potential genetic risk associated with occupational exposure to mutagens.","","","RefMan","","","","","","","","","" "Unknown","Unknown","Unknown","Unknown","","","2007","Djadid, N. D., Forouzesh, F., Karimi, M., Raeisi, A., Hassan-Zehi, A., Zakeri, S.","Monitoring pyrethroid insecticide resistance in major malaria vector Anopheles culicifacies: comparison of molecular tools and conventional susceptibility test","Iranian biomedical journal","11(3):169-76","bc41fabd-7795-4c93-951f-53b35a554349","","BACKGROUND: Anopheles culicifacies is a main malaria vector in southeastern part of Iran, bordring Afghanistan and Pakistan. So far, resistance to DDT, dieldrin, malathion and partial tolerance to pyrethroids has been reported in An. stephensi, but nothing confirmed on resistance status of An. culicifacies in Iran. METHODS: In current study, along with WHO routine susceptibility test with DDT (4%), dieldrin (0.4%), malathion (5%), permethrin (0.25%), lambadacyhalothrin (0.1%), and deltamethrin 0.025, we cloned and sequenced segment VI of domain II (SII6) in voltage-gated sodium channel (vgsc) gene of An. culicifacies specimens collected in Sistan and Baluchistan province (Iran). RESULTS: A 221-bp amplified fragment showed 91% and 93% similarity with exon I and exon II of An. gambiae. The size of intron II in An. culicifacies is 62 bp, while in An. gambiae is 57 bp. The major difference within An. culicifacies specimens and also with An. gambiae is in position 29 of exon I, which led to substitution of Leu to His amino acid. CONCLUSION: This data will act as first report on partial sequence of vgsc gene and its polymorphism in An. culicifacies. A Leu to His amino acid substitution detected upstream the formerly known knockdown resistance (kdr) mutation site could be an indication for other possible mutations related to insecticide resistance. However, the

result of WHO susceptibility test carried out in Baluchistan of Iran revealed a level of tolerance to DDT and dieldrin, but almost complete susceptibility to pyrethroids in An. culicifacies. We postulate that the molecular diagnostic tool developed for detection and identification of kdr-related mutations in An. culicifacies, could be useful in monitoring insecticide resistance in Iran and neighbouring countries such as Pakistan and Afghanistan. A phylogenetic tree also constructed based on the sequence of exon I and II, which readily separated An. culicifacies populations from An. stephensi, An. fluviatilis and An. gambiae.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","2011","Djouaka, R., Irving, H., Tukur, Z., Wondji, C. S.","Exploring mechanisms of multiple insecticide resistance in a population of the malaria vector Anopheles funestus in Benin","PloS one","6(11):e27760","c6190611-9d55-465e-9ac2-d9630231bf57","","BACKGROUND: The insecticide resistance status of the malaria vector Anopheles funestus and the underlying resistance mechanisms remain uncharacterised in many parts of Africa, notably in Benin, West Africa. To fill this gap in our knowledge, we assessed the susceptibility status of a population of this species in Pahou, Southern Benin and investigated the potential resistance mechanisms. METHODOLOGY/PRINCIPAL FINDINGS: WHO bioassays revealed a multiple resistance profile for An. funestus in Pahou. This population is highly resistant to DDT with no mortality in females after 1h exposure to 4%DDT. Resistance was observed against the Type I pyrethroid permethrin and the carbamate bendiocarb. A moderate resistance was detected against deltamethrin (type II pyrethroids). A total susceptibility was observed against malathion, an organophosphate. Pre-exposure to PBO did not change the mortality rates for DDT indicating that cytochrome P450s play no role in DDT resistance in Pahou. No L1014F kdr mutation was detected but a correlation between haplotypes of two fragments of the Voltage-Gated Sodium Channel gene and resistance was observed suggesting that mutations in other exons may confer the knockdown resistance in this species. Biochemical assays revealed elevated levels of GSTs and cytochrome mono-oxygenases in Pahou. No G119S mutation and no altered acetylcholinesterase gene were detected in the Pahou population. qPCR analysis of five detoxification genes revealed that the GSTe2 is associated to the DDT resistance in this population with a significantly higher expression in DDT resistant samples. A significant over-expression of CYP6P9a and CYP6P9b previously associated with pyrethroid resistance was also seen but at a lower fold change than in southern Africa. CONCLUSION: The multiple insecticide resistance profile of this An. funestus population in Benin shows that more attention should be paid to this important malaria vector for the implementation and management of current and future malaria vector control programs in this country.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","2012","Durand, R., Bouvresse, S., Berdjane, Z., Izri, A., Chosidow, O., Clark, J. M.","Insecticide resistance in head lice: clinical, parasitological and genetic aspects","Clinical microbiology and infection : the official publication of the European Society of Clinical Microbiology and Infectious Diseases","18(4):338-44","5364beeb-de4b-4cea-a3f2-0c23149b4ca5","","Insecticide treatment resistance is considered to be a major factor in the increasing number of infestations by head lice. The large insecticide selection pressure induced by conventional topical pediculicides has led to the emergence and spread of resistance in many parts of the world. Possible mechanisms of resistance include accelerated detoxification of insecticides by enzyme-mediated reduction,

esterification, oxidation that may be overcome by synergistic agents such as piperonyl butoxide, alteration of the binding site, e.g. altered acetylcholinesterase or altered nerve voltage-gated sodium channel, and knockdown resistance (kdr). Clinical, parasitological and molecular data on resistance to conventional topical pediculicides show that treatments with neurotoxic insecticides have suffered considerable loss of activity worldwide. In particular, resistance to synthetic pyrethroids has become prominent, probably because of their extensive use. As other treatment options, including non-insecticidal pediculicides such as dimeticone, are now available, the use of older insecticides, such as lindane and carbaryl, should be minimized, owing to their loss of efficacy and safety concerns. The organophosphorus insecticide malathion remains effective, except in the UK, mostly in formulations that include terpineol.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","2007","Durand, R., Millard, B., Bouges-Michel, C., Bruel, C., Bouvresse, S., Izri, A.","Detection of pyrethroid resistance gene in head lice in schoolchildren from Bobigny, France","Journal of medical entomology","44(5):796-8","b5d2b546-e901-47f2-9fb9-2e195838f8a9","","The head louse, Pediculus humanus capitis (De Geer), is an hematophagous ectoparasite that affects mainly children. Resistance to insecticides belonging to pyrethroids and other pediculicides, such as malathion, is responsible for frequently reported treatment failures. Recent studies showed that a M815I-T929I-L932F kdr-like mutation in the voltage-gated sodium channel alpha-subunit gene was associated with permethrin resistance in head lice from several countries worldwide. We searched for the presence ofpyrethroid resistance gene in head lice populations obtained in schoolchildren in an urban area of France. All the 15 primary schools of Bobigny, a city located 3 km north of Paris, were selected to participate. Of 3,493 children enrolled, 3,345 (95.8%) children were screened for head lice by using fine-toothed antilouse combs. Live head lice were detected in 112 (3.3%) of children screened. A subsample of 90 lice was processed for DNA study. The amplification of a 332-bp portion of the kdr-like gene spanning the codon 929 was performed, and polymerase chain reaction products were submitted to the restriction enzyme SspI. Twenty of these lice (22.2%) were homozygous susceptible, 33 (36.7%) were homozygous resistant, and 37 (41.1%) were heterozygotes. Globally, the frequency of the T929I mutation was 0.57. The prevalence of pediculosis in schoolchildren of Bobigny seemed relatively low in comparison with findings of other European studies. The presence of the T929I mutation associated with permethrin resistance probably reflected the frequent local use of this insecticide. Further studies are now required to evaluate the prevalence of the kdr-like mutant allele in head lice in French schools.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","2003","Enayati, A. A., Vatandoost, H., Ladonni, H., Townson, H., Hemingway, J.","Molecular evidence for a kdr-like pyrethroid resistance mechanism in the malaria vector mosquito Anopheles stephensi","Medical and veterinary entomology","17(2):138-44","841c9e33-7107-4eb6-9033-aee3e1ca55c5","","The mosquito Anopheles stephensi Liston (Diptera: Culicidae) is the urban vector of malaria in several countries of the Middle East and Indian subcontinent. Extensive use of residual insecticide spraying for malaria vector control has selected An. stephensi resistance to DDT, dieldrin, malathion and other organophosphates throughout much of its range and to pyrethroids in the Middle East. Metabolic resistance mechanisms and insensitivity to pyrethroids, so-called knockdown resistance (kdr), have previously been reported in An. stephensi. Here we provide molecular data supporting the

hypothesis that a kdr-like pyrethroid-resistance mechanism is present in An. stephensi. We found that larvae of a pyrethroid-selected strain from Dubai (DUB-R) were 182-fold resistant to permethin, compared with a standard susceptible strain of An. stephensi. Activities of some enzymes likely to confer pyrethroid-resistance (i.e. esterases, monooxygenases and glutathione S-transferases) were significantly higher in the permethrin-resistant than in the susceptible strain, but the use of synergists--piperonyl butoxide (PBO) to inhibit monooxygenases and/or tribufos (DEF) to inhibit esterases--did not fully prevent resistance in larvae (permethrin LC50 reduced by only 51-68%), indicating the involvement of another mechanism. From both strains of An. stephensi, we obtained a 237-bp fragment of genomic DNA encoding segment 6 of domain II of the para type voltage-gated sodium channel, i.e. the putative kdr locus. By sequencing this 237 bp fragment, we identified one point mutation difference involving a single A-T base change encoding a leucine to phenylalanine amino acid substitution in the pyrethroid-resistant strain. This mutation appears to be homologous with those detected in An. gambiae and other insects with kdr-like resistance. A diagnostic polymerase chain reaction assay using nested primers was therefore designed to detect this mechanism in An. stephensi.","","","RefMan","","","","","","","","","","Unknown","Unknown","Unknown","Unknown","","","2005","Espinoza-Navarro, O., Bustos-Obregon, E.","Effect of malathion on the male reproductive organs of earthworms, Eisenia foetida","Asian journal of andrology","7(1):97-101","65ef1b10-f48e-48db-8c1b-044ef50b9a89","","AIM: To observe the cytotoxic effect of the organophosphate insecticide malathion in the reproductive tissues of the earthworms, Eisenia foetida. METHODS: Worms were nourished in soil treated with malathion at single sub-lethal doses of 0, 80, 150, 300 and 600 mg/kg soil. (LD50=880 mg/kg soil) and evaluated on days 1, 5, 15 and 30 after exposure. The body weights were recorded and male reproductive organs evaluated. RESULTS: Malathion-treated animals showed a significant reduction in body weight in a dose-dependent manner. Malathion treatment modified the disposition of spermatozoa in the basal epithelium of the spermatheca. The Br-deoxyuridine test showed a significant rise in cells in phase S on days 5 and 15. Also, a higher percentage of spermatogonia with fragmented DNA were observed by means of the TdT-mediated dUTP nick-end labeling (TUNEL) technique in the spermatheca of treated animals. CONCLUSION: Treatment with malathion decreased the body weight and the spermatic viability in spermatheca, altering the cell proliferation and modifying the DNA structure of spermatogonia.","","","RefMan","","","","","","","","","","Unknown","Unknown","Unknown","Unknown","","","2015","Etchepare, R., van der Hoek, J. P.","Health risk assessment of organic micropollutants in greywater for potable reuse","","72:186-198","ffc0d041-953f-4a8e-ac22-9bf0a9284ec5","","In light of the increasing interest in development of sustainable potable reuse systems, additional research is needed to elucidate the risks of producing drinking water from new raw water sources. This article investigates the presence and potential health risks of organic micropollutants in greywater, a potential new source for potable water production introduced in this work. An extensive literature survey reveals that almost 280 organic micropollutants have been detected in greywater. A three-tiered approach is applied for the preliminary health risk assessment of these chemicals. Benchmark values are derived from established drinking water standards for compounds grouped in Tier 1, from literature toxicological data for compounds in Tier 2, and from a Threshold of Toxicological Concern approach for compounds in Tier 3. A risk quotient is estimated by comparing the maximum concentration levels reported in greywater to the benchmark

values. The results show that for the majority of compounds, risk quotient values were below 0.2, which suggests they would not pose appreciable concern to human health over a lifetime exposure to potable water. Fourteen compounds were identified with risk quotients above 0.2 which may warrant further investigation if greywater is used as a source for potable reuse. The present findings are helpful in prioritizing upcoming greywater quality monitoring and defining the goals of multiple barriers treatment in future water reclamation plants for potable water production.","","","RefMan","","","","","","","","","","","Unknown","Unknown","Unknown","Unknown","","","2007","Ffrench-Constant, R. H.","Which came first: insecticides or resistance?","Trends in genetics : TIG","23(1):1-4","5b89fc9b-6132-4f92-b2c4-6a17b2efed0a","","Mutations that confer resistance to insecticides are well documented. However, so far, we have been unable to determine whether these mutations arose before or after the introduction of insecticides. Recently, a landmark study showed that resistance to Malathion can be detected in pinned specimens of Australian sheep blowflies that were collected before the introduction of the insecticide. This finding has numerous implications for our understanding of the prevalence of resistance to new compounds. It also indicates that pre-existing resistance alleles might not carry the fitness cost that is associated with new mutations.","","","RefMan","","","","","","","","","","","Unknown","Unknown","Unknown","Unknown","","","2015","Galal, A. F., Abdel Razik, T. E., El-Bana, M. A.","The protective effect of creatine supplements against malathion-induced neuro and liver toxicity","","7(5):203-214","af7023e4-5a16-47ed-b881-fa6ce9489f21","","The aim of this study was to investigate the effect of treatment with creatine on the neuro and hepatotoxic effects of acute malathion exposure. Rats received malathion (150 mg/kg, i.p. injection) for two successive days either alone or combined with creatine at doses of 160, 360 or 720 mg/kg, orally. Serum acetylcholine esterase (AChE), butyryl cholinesterase (BuChE) and paraoxonase-1 (PON1) activities were determined in addition to comet assay. Malondialdehyde (MDA), reduced glutathione (GSH), superoxide dismutase (SOD) activity and nitric oxide (NO) were determined in brain and liver tissues. Serum BuChE, AChE and PON1 activities were inhibited after the administration of malathion. Malathion resulted in an increase in MDA, NO; a decrease in GSH level and SOD activity in both brain and liver tissues. Malathion also caused marked increase in DNA damage of peripheral blood lymphocytes. These effects of malathion were ameliortaed with the administration of creatine. Our data indicate that creatine protects against malathion neuro and hepatic adverse effects, most likely through direct antioxidant mechanism and up regulation of antioxidant defense systems.","","","RefMan","","","","","","","","","","","Unknown","Unknown","Unknown","Unknown","","","2011","Galantai, R., Emody-Kiss, B., Somosy, Z., Bognar, G., Horvath, G., Forgacs, Z., Gachalyi, A., Szilasi, M.","Does malaoxon play a role in the geno- and cytotoxic effects of malathion on human choriocarcinoma cells?","Journal of environmental science and health. Part. B, Pesticides, food contaminants, and agricultural wastes","46(8):773-9","0b58ed0e-79c1-467c-8c03-5712ae9de160","","This investigation was undertaken to elucidate whether the active metabolite of malathion, malaoxon, has any role in exerting cyto- and genotoxic effects for human choriocarcinoma (JAR) cell line which is an acceptable model for human placental cells. Gas chromatography-mass spectrometry (GC-MS) analysis were separately performed on the cell compartment and supernatant cell culture medium after subjecting the cell line to different malathion concentrations (10-400 mug/mL) and for

various incubation periods (0.5 to 24 hours). GC-MS analysis showed that the sonication performed for the disruption of the cells did not cause the chemical change of malathion. The uptake of malathion by the cells was relatively fast. However, the presence of malaoxon, even in trace amounts, could not be confirmed either in samples originating from disrupted cells or in the cell culture medium. Although the hydrolysis of malaoxon occurred in the culture medium, this degradation process could not be counted as a reason for the absence of malaoxon. Since both malathion and malaoxon standard compounds could be accurately detected and distinguished by the applied liquid-liquid extraction and GC-MS methods, one can conclude that, in the case of JAR cells, the parent compound, (i.e. malathion itself) is responsible for the observed in vitro cyto- and genotoxic effects. Our results indicate that the direct toxicity of malathion contributes to the complications of pregnancy observed for environmental malathion exposure.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","2002","Galindo Reyes, J. G., Leyva, N. R., Millan, O. A., Lazcano, G. A.","Effects of pesticides on DNA and protein of shrimp larvae Litopenaeus stylirostris of the California Gulf","Ecotoxicology and environmental safety","53(2):191-5","badc0417-f8a4-45a3-ac49-67c36ef233d4","","Recently, diverse pathologies and massive mortalities have been presented in shrimp hatcheries located along the California Gulf; therefore, toxic responses of shrimp larvae were used as biomarkers of pesticide pollution, because in this region intensive agriculture is practiced. Shrimp larvae were exposed to DDT, azinphosmethyl, permethrine, parathion, chlorpyrifos, malathion, endosulfan, and carbaryl, in order to determine LC50, DNA adducts and/or breaks, and total protein in larvae. The results indicate reductions in protein and DNA in larvae exposed to these pesticides, and in those exposed to DDT, breaks and/or adducts were registered. It is possible that pesticide pollution is a cause of these problems, because reduction in protein indicates a decrease in larvae growth rate and DNA breaks or adducts have been related to pathologies and carcinogenesis in many aquatic organisms.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","2013","Gao, X. M., Jia, F. X., Shen, G. M., Jiang, H. Q., Dou, W., Wang, J. J.","Involvement of superoxide dismutase in oxidative stress in the oriental fruit fly, Bactrocera dorsalis: molecular cloning and expression profiles","Pest management science","69(12):1315-25","2edc8176-bec7-4cbb-85bf-7dab967bf7ae","","BACKGROUND: Bactrocera dorsalis, one of the most economically important fruit fly pests in East Asia, is well adapted to various environmental conditions. Pesticides, pathogens and other stresses can cause oxidative damage in most organisms. The superoxide dismutase (SOD) family contains some of the most important enzymes in the antioxidant protection system of the fruit fly and other organisms. RESULTS: Four full-length cDNA sequences encoding one MnSOD (BdSOD2-1) and three Cu-ZnSODs (BdSOD1-1, BdSOD1-2 and BdSOD1-3) were cloned. The expression profiles of these four genes under different stresses showed them to be involved in response to detrimental conditions including heavy metals, pesticides, extreme temperatures and lipopolysaccharide (LPS) stresses. More specifically, the expression levels of these genes were found to be depressed in the presence of copper, zinc and manganese. The expression of all four SOD genes increased upon exposure to lead, cadmium, low temperature (0 degrees C) and LPS stresses. Only BdSOD1-3 transcription increased significantly at high temperature (40 degrees C) exposure. The expressions levels of BdSOD1-2 and BdSOD1-3 increased significantly in the presence of beta-cypermethrin and

malathion, but only the expression of BdSOD2-1 increased in the presence of avermectin treatment. CONCLUSION: These different expression profiles suggest that the four BdSODs play different roles and respond to different oxidative stresses in B. dorsalis. Some BdSODs undergo specific reaction in the response to specific oxidative stresses.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","2001","Garaj-Vrhovac, V., Zeljezic, D.","Cytogenetic monitoring of croatian population occupationally exposed to a complex mixture of pesticides","Toxicology","165(2-3):153-62","f342fbcf-26b6-4623-9e66-fd2a68f6ade9","","This paper describes a longitudinal study of possible genetic damage in Croatian workers occupationally exposed to a complex mixture of pesticides. The methods of choice were chromosomal aberration analysis, sister chromatid exchange analysis (SCE), micronucleus assay and comet assay. In order to determine primary genotoxic effects in workers, blood samples were taken after the workers spent 8 months in the production of pesticides. During the production all subjects were simultaneously exposed to a complex mixture of pesticides containing atrazine, alachlor, cyanazine, 2,4-dichlorophenoxyacetic acid, and malathion. To detect DNA repair in lymphocytes of the same subjects the second series of blood samples was taken 8 months after the workers were removed from production. Regardless of the time sampling time the exposed workers showed an increased number of chromosomal aberrations, SCE frequency, micronucleus (MN) frequency, and values of comet assay parameters. After 8 months of non-exposure the workers showed a significantly decreased number of chromosomal aberrations, MN frequency, and DNA migration compared to the results of the first sampling, but it was still significantly higher than in controls. Furthermore, the SCE frequency in the exposed subjects did not drop after the 8 months of non-exposure, which indicates long-term exposure to a mixture of pesticides.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","2002","Garaj-Vrhovac, V., Zeljezic, D.","Assessment of genome damage in a population of Croatian workers employed in pesticide production by chromosomal aberration analysis, micronucleus assay and Comet assay","Journal of applied toxicology : JAT","22(4):249-55","b2db5688-f2c7-4f13-a73f-1f85d47f3b5d","","The widespread use of pesticides suggests that the evaluation of their genotoxicity should be extended using the different assays available. In the present study we used two standard cytogenetic methods (chromosomal aberration analysis and micronucleus assay) and the Comet assay as a relatively new and powerful technique. The study included 10 workers occupationally exposed to a complex mixture of pesticides (atrazine, alachlor, cyanazine, 2,4-dichlorophenoxyacetic acid, malathion) during their production and 20 control subjects with no history of exposure to any physical or chemical agents. For the chromosomal aberration analysis, whole blood was cultivated for 48 h, whereas for the micronucleus assay, whole blood was cultivated for 72 h. For the comet assay whole blood was embedded in agarose on a microscope slide, lysed with detergent, denaturated and subjected to alkaline electrophoresis. Damage to DNA was evaluated by measuring tail length and calculating the tail moment. A significantly increased number of chromatid and chromosome breaks, as well as the presence of dicentric chromosomes and chromatid exchanges in exposed subjects compared with control subjects ($P < 0.05$), was found. There was also a statistically significant difference in frequency and distribution of micronuclei between the two groups examined. In the exposed subjects the Comet assay showed a statistically significant ($P < 0.001$) increase in DNA migration. Results suggest that long-term occupational exposure to

pesticides could cause genome damage in somatic cells and therefore may represent a potential hazard to human health.","","","RefMan","","","","","","","","","" "Unknown","Unknown","Unknown","Unknown","","","2006","Gayathri, V., Balakrishna Murthy, P.","Reduced susceptibility to deltamethrin and kdr mutation in Anopheles stephensi Liston, a malaria vector in India","","22(4):678-688","50493ed7-9252-40bb-a451-ab0bda979d9d","","The Indian urban malaria vector Anopheles stephensi Liston was selected for deltamethrin resistance for 25 generations (F25) at larval and adult stages separately in the laboratory. There was roughly a 151-fold increase in the lethal concentration (LC)50 and a 99-fold increase in the LC 90 in larval selection, when the F25 was compared with the parent colony. Similarly, adult selection resulted in a 39-fold increase in the LC50 and a 31-fold increase in the LC90 in the adults. Knockdown bioassays conducted on adults (selected at the larval and adult stages) against the diagnostic concentration of insecticide-impregnated papers, namely, deltamethrin (0.05%), permethrin (0.75%), Î»-cyhalothrin (0.05%), and cyfluthrin (0.15%), revealed that the adults selected at the adult stage were more resistant to deltamethrin and the other pyrethroids than those selected at the larval stage. A significant cross-resistance to DDT was noticed only in the adults selected at the adult stage, and no cross-resistance to malathion and propoxur was observed in the adults of both resistant colonies. Polymerase chain reaction studies revealed an occurrence of heterozygote level of kdr mutation (leucine to phenylalanine) in the adults selected at the adult stage. This event was not observed in the adults selected at the larval stage. Moreover, this is the first report on the occurrence of kdr mutation in Indian An. stephensi resistant to deltamethrin. Copyright Â© 2006 by The American Mosquito Control Association, Inc.","","","RefMan","","","","","","","","","" "Unknown","Unknown","Unknown","Unknown","","","2011","Giri, A., Giri, S., Sharma, G. D.","Malathion and fenvalerate induce micronuclei in mouse bone marrow cells","Environmental and molecular mutagenesis","52(8):607-13","cc65cd1c-deca-4d61-8b2c-f8f469417700","","Health effects of pesticides are a major public health concern. In this study, the genotoxic effects of two commonly-used pesticides, malathion, and fenvalerate, were investigated in mice in vivo. Induction of micronuclei in bone marrow cells was used as the test parameter following exposure to 2.5, 5 or 10 mg/kg malathion by intraperitoneal (i.p.) or per oral (p.o.) exposure. Exposure by both routes was found to cause a significant increase in micronucleated polychromatic erythrocytes (PCEs) in a dose-dependent manner ($r = 0.9769$; $P < 0.05$). The highest dose (10 mg/kg) induced significant ($P < 0.05$) cytotoxicity. In contrast, fenvalerate caused an increase in micronucleated PCEs only at higher doses (10 and 20 mg/kg) via i.p. injection, and was not associated with cytotoxicity. A significant dose-response correlation was not observed in the dose ranges tested for fenvalerate ($r = 0.8704$; $P > 0.05$). The results suggest that technical grade malathion is a genotoxic agent. In contrast, technical grade fenvalerate appears to be a potent genotoxic agent, but this observation should be confirmed with further investigation(s).","","","RefMan","","","","","","","","","" "Unknown","Unknown","Unknown","Unknown","","","2012","Giri, A., Yadav, S. S., Giri, S., Sharma, G. D.","Effect of predator stress and malathion on tadpoles of Indian skittering frog","Aquatic toxicology (Amsterdam, Netherlands)","106-107:157-63","8aa068c8-76f8-48a3-bf64-5c6e21422ea2","","The impact of pesticides on amphibians is of particular concern because their populations appear to be declining on a global scale. We examined the toxic and genotoxic effects of malathion, a commonly used

organophosphorus pesticide, in the larvae of Indian skittering frog (Euflictis cyanophlyctis). The different concentrations of malathion (0, 0.5, 1.0, 2.0, 4.0 and 8.0mg/L) tested in a 2x6 factorial design, induced concentration-dependent lethality in tadpoles in the presence and absence of predator cues. The 96 h LC50 for malathion in the presence and absence of predator stress were 3.523 mg/L and 3.588 mg/L, respectively. The 15-day LC50 value for malathion was estimated to be 2.452 mg/L. Lower concentrations of malathion extending into the sublethal range (0.5, 1.0 and 2.0 mg/L) induced micronuclei (MN) in the erythrocytes of tadpoles at 24 h (F(3),(5)(6)=70.291, p<0.001), 48 h (F(3),(5)(6)=78.423, p<0.001), 72 h (F(3),(5)(6)=88.817, p<0.001) and 96 h (F(3),(5)(6)=64.770, p<0.001) in a concentration-dependent manner. Predator stress significantly enhanced the MN frequency at 48 h following 1.0mg/L malathion treatment (p<0.001). The present report is the first one to analyze genotoxic effect of malathion in the presence of predator stress. These results suggest that predator stress may potentiate the genotoxic effect of lower concentrations of malathion in E. cyanophlyctis tadpoles. These effects may have long-term fitness consequence to the population as a whole.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","2002","Giri, S., Prasad, S. B., Giri, A., Sharma, G. D.","Genotoxic effects of malathion: an organophosphorus insecticide, using three mammalian bioassays in vivo","Mutation research","514(1-2):223-31","73703766-0d59-41bd-b212-bf1128688e00","","The genotoxic effects of malathion was evaluated using chromosome aberration, sister chromatid exchange (SCE) and sperm abnormality assays in mice. All the three acute doses (2.5, 5 and 10mg/kg) of malathion tested in the present study, induced significant dose-dependent increase in the frequency of chromosome aberrations and sperm abnormalities, but did not affect the total sperm count. The highest acute dose induced a >12-fold increase in the frequency of chromosome aberrations, two-fold increase in the frequency of SCEs and four-fold increase in the frequency of sperms with abnormal head morphology following intraperitoneal (i.p.) exposure. Further, a significant increase in the frequency of SCEs was observed, but the increase was not dose-dependent. At higher doses, malathion induced a moderate delay in cell cycle as evident from the increase in average generation time (AGT). The present findings suggest that technical grade malathion is a potent genotoxic agent and may be regarded as a potential germ cell mutagen also.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","2009","Greim, H., Hartwig, A., Reuter, U., Richter-Reichhelm, H. B., Thielmann, H. W.","Chemically induced pheochromocytomas in rats: Mechanisms and relevance for human risk assessment","","39(8):695-718","801d1dec-7351-418f-9db7-879c1a4bd176","","Pheochromocytomas are tumors originating from chromaffin cells of the adrenal medulla, which have been observed in numerous carcinogenicity studies. The authors have evaluated pheochromocytoma concurrence with other effects and the possible mechanisms, in order to assess the relevance of such data for the classification of carcinogenic effects and their relevance to humans. The evaluation revealed that pheochromocytomas occur with relatively higher frequency in male rats, especially when the following conditions are involved: hypoxia, uncoupling of oxidative phosphorylation, disturbance in calcium homeostasis, and disturbance of the hypothalamic endocrine axis. The underlying biochemical mechanisms suggest that other substances that interfere with these biochemical endpoints also produce pheochromocytomas. Such endpoints include enzymes involved in catecholamine synthesis, receptor tyrosine kinase (RET), hypoxia-inducible

factor (HIF), succinate dehydrogenase, fumarate hydratase, and pyruvate dehydrogenase. To date, there is no indication that the substances inducing pheochromocytomas in animal experiments also induce corresponding tumors in humans. Because the mechanisms of action identified in rats are to be expected in humans, pheochromocytomas may be induced after exposure conditions similar to those used in the animal studies. Whether hereditary mutations represent a risk factor in humans is not clear. Pheochromocytomas that occur in animal experiments currently appear to have little relevance for conditions at the work place. When sufficiently documented and evaluated, such secondary pheochromocytomas are not relevant for classification and human risk assessment. Â© 2009 Informa UK Ltd.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","2006","Guest, R. K., Ikehata, K., El-Din, M. G., Smith, D. W.","Pesticides and herbicides","","78(10):1755-1801","8d636871-fe37-4a5e-8975-3f2975d9e5fe","","","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","2015","Guyton, K. Z., Loomis, D., Grosse, Y., El Ghissassi, F., Benbrahim-Tallaa, L., Guha, N., Scoccianti, C., Mattock, H., Straif, K., Blair, A., Fritschi, L., McLaughlin, J., Sergi, C. M., Calaf, G. M., Le Curieux, F., Baldi, I., Forastiere, F., Kromhout, H., t Mannetje, A., Rodriguez, T., Egeghy, P., Jahnke, G. D., Jameson, C. W., Martin, M. T., Ross, M. K., Rusyn, I., Zeise, L.","Carcinogenicity of tetrachlorvinphos, parathion, malathion, diazinon, and glyphosate","","16(5):490-491","df69cf06-d520-4af5-a804-a6c3fc71d566","","","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","2008","Gwinn, M. R., Weston, A.","Application of oligonucleotide microarray technology to toxic occupational exposures","Journal of toxicology and environmental health. Part A","71(5):315-24","8e2bd374-d9fa-4f9c-9d28-bd23e28f77aa","","Microarray technology has advanced toward analysis of toxic occupational exposures in biological systems. Microarray analysis is an ideal way to search for biomarkers of exposure, even if no specific gene or pathway has been identified. Analysis may now be performed on thousands of genes simultaneously, as opposed to small numbers of genes as in the past. This ability has been put to use to analyze gene expression profiles of a variety of occupational toxins in animal models to classify toxins into specific categories based on response. Analysis of normal human cell strains allows an extension of this analysis to investigate the role of interindividual variation in response to various toxins. This methodology was used to analyze four occupationally related toxins in our lab: oxythioquinox (OTQ), a quinoxaline pesticide; malathion, an organophosphate pesticide; di-n-butyl phthalate (DBP), a chemical commonly found in personal care and cosmetic items; and benzo[a]pyrene (BaP), an environmental and occupational carcinogen. The results for each exposure highlighted signaling pathways involved in response to these occupational exposures. Both pesticides showed increase in metabolic enzymes, while DBP showed alterations in genes related to fertility. BaP exposure showed alterations in two cytochrome P450s related to carcinogenicity. When used with occupational exposure information, these data may be used to augment risk assessment to make the workplace safer for a greater proportion of the workforce, including individuals susceptible to disease related to exposures.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","2014","Hamouzova, K., Kosnarova, P., Salava, J., Soukup, J., Hamouz, P.","Mechanisms of resistance to acetolactate synthase-inhibiting herbicides in populations of Apera spica-venti from the Czech Republic","Pest management science","70(4):541-8","cfb7d3df-3010-48f9-8844-

a65dd1ca5a78","","BACKGROUND: This study investigates the mechanisms of resistance to acetolactate synthase-inhibiting herbicides in populations of Apera spica-venti (L.) P.B. from the Czech Republic. RESULTS: The proportion of resistance due to mutant acetolactate synthase (ALS) alleles was estimated by genotyping individuals from each of three populations for the eight ALS mutations known to confer resistance. Four resistance-conferring ALS mutations were identified: Pro-197-Ala, Pro-197-Thr, Trp-574-Leu and previously unreported Trp-574-Met substitution. Two populations (R1, R3) have amino acid substitution at positions Pro-197 and Trp-574. Individuals from the R3 population had two different resistance alleles. In the R2 population, only the resistant Trp-574-Met substitution was detected. Ten other single point mutations were identified, but these were not related to resistance. The cytochrome malathion decreased chlorsulfuron resistance in the resistant populations that were examined. Although malathion increased mortality, the GR50 values were too high to conclude that non-target-based mechanism was the main one for the resistance in Apera spica-venti populations tested in this study. CONCLUSIONS: Individuals of Apera spica-venti populations tested in this study possess the target-site ALS resistance mutation and an additional so far unknown resistance
mechanism(s).","","","RefMan","","","","","","","","","",""
"Unknown","Unknown","Unknown","Unknown","","","2006","Hartley, C. J., Newcomb, R. D., Russell, R. J., Yong, C. G., Stevens, J. R., Yeates, D. K., La Salle, J., Oakeshott, J. G.","Amplification of DNA from preserved specimens shows blowflies were preadapted for the rapid evolution of insecticide resistance","Proceedings of the National Academy of Sciences of the United States of America","103(23):8757-62","23daf91c-1c4a-4cd1-b934-71ff22631f6a","","Mutations of esterase 3 confer two forms of organophosphate resistance on contemporary Australasian Lucilia cuprina. One form, called diazinon resistance, is slightly more effective against commonly used insecticides and is now more prevalent than the other form, called malathion resistance. We report here that the single amino acid replacement associated with diazinon resistance and two replacements associated with malathion resistance also occur in esterase 3 in the sibling species Lucilia sericata, suggesting convergent evolution around a finite set of resistance options. We also find parallels between the species in the geographic distributions of the polymorphisms: In both cases, the diazinon-resistance change is absent or rare outside Australasia where insecticide pressure is lower, whereas the changes associated with malathion resistance are widespread. Furthermore, PCR analysis of pinned specimens of Australasian L. cuprina collected before the release of organophosphate insecticides reveals no cases of the diazinon-resistance change but several cases of those associated with malathion resistance. Thus, the early outbreak of resistance in this species can be explained by the preexistence of mutant alleles encoding malathion resistance. The pinned specimen analysis also shows much higher genetic diversity at the locus before organophosphate use, suggesting that the subsequent sweep of diazinon resistance in Australasia has compromised the scope for the locus to respond further to the ongoing challenge of the
insecticides.","","","RefMan","","","","","","","","","",""
"Unknown","Unknown","Unknown","Unknown","","","2009","Hayashi, Y.","Scientific basis for risk analysis of food-related substances with particular reference to health effects on children","","34(2 SPEC. ISS.):SP201-SP207","fac94933-982e-42a9-9665-74e87e321479","","Based on the advance of toxicology and related sciences, a regulatory regime for the safety of chemicals related to daily life has been rapidly established.

Especially for the food-related substances, the process of risk analysis has facilitated the collaboration by all the players including consumers toward the security of their safety. On the other hand, except for pharmaceuticals, science-based decisions and governmental actions on safety issues have not always gained confidence of the public. One of the reasons was the inadequacy in the way of use of scientific knowledge, or in other words, inappropriateness of decision making by ""the regulatory science"". Regulatory science is a science to warrant the decision making processes for governmental acts (Mitsuru Uchiyama). In the case of chemical safety, it can be redefined as a theoretical concept to complements the uncertainty of scientific knowledge for the decision of governmental acts that is adequate in both scientific and social ways. Therefore, the regulatory science is an indispensable discipline to effectively apply risk analysis. Here, the significance of the regulatory science for the hazard assessment of the chemicals, especially for children is described. In the past, the hazard effects of chemicals have been assessed for adults. Recently, however, the importance of the assessment for children has gained international emphases. Not only for pharmaceuticals, but for food-related substances, the acceptable daily intake (ADI) and tolerable daily intake (TDI) are often set differently for adults and children. The child-specific responses against chemicals are related not only to the physiological factors such as body weight, basal metabolism, but also rapid growth of the body with developmental status of various organs. General knowledge on these issues will be discussed mainly referring the World Health Organization (WHO) documents. Although the cutting edge technology backs up the development of toxicology, it would appear that it is reaching a turning point from technology-centrism to look toward the direction for contribution to society from the stand point of regulatory science.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","2004","Heidari, R., Devonshire, A. L., Campbell, B. E., Bell, K. L., Dorrian, S. J., Oakeshott, J. G., Russell, R. J.","Hydrolysis of organophosphorus insecticides by in vitro modified carboxylesterase E3 from Lucilia cuprina","Insect biochemistry and molecular biology","34(4):353-63","876556d6-983d-4d64-919e-33c9dbc0a44c","","Resistance of the blowfly, Lucilia cuprina, to organophosphorus (OP) insecticides is due to mutations in LcalphaE7, the gene encoding carboxylesterase E3, that enhance the enzyme's ability to hydrolyse insecticides. Two mutations occur naturally, G137D in the oxyanion hole of the esterase, and W251L in the acyl binding pocket. Previous in vitro mutagenesis and expression of these modifications to the cloned gene have confirmed their functional significance. G137D enhances hydrolysis of diethyl and dimethyl phosphates by 55- and 33-fold, respectively. W251L increases dimethyl phosphate hydrolysis similarly, but only 10-fold for the diethyl homolog; unlike G137D however, it also retains ability to hydrolyse carboxylesters in the leaving group of malathion (malathion carboxylesterase, MCE), conferring strong resistance to this compound. In the present work, we substituted these and nearby amino acids by others expected to affect the efficiency of the enzyme. Changing G137 to glutamate or histidine was less effective than aspartate in improving OP hydrolase activity and like G137D, it diminished MCE activity, primarily through increases in Km. Various substitutions of W251 to other smaller residues had a broadly similar effect to W251L on OP hydrolase and MCE activities, but at least two were quantitatively better in kinetic parameters relating to malathion resistance. One, W251G, which occurs naturally in a malathion resistant hymenopterous parasitoid, improved MCE activity more than 20-fold. Mutations at other sites near the

bottom of the catalytic cleft generally diminished OP hydrolase and MCE activities but one, F309L, also yielded some improvements in OP hydrolase activities. The results are discussed in relation to likely steric effects on enzyme-substrate interactions and future evolution of this gene.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","2005","Heidari, R., Devonshire, A. L., Campbell, B. E., Dorrian, S. J., Oakeshott, J. G., Russell, R. J.","Hydrolysis of pyrethroids by carboxylesterases from Lucilia cuprina and Drosophila melanogaster with active sites modified by in vitro mutagenesis","Insect biochemistry and molecular biology","35(6):597-609","97263c36-4164-4315-9962-754bdd015136","","The cloned genes encoding carboxylesterase E3 in the blowfly Lucilia cuprina and its orthologue in Drosophila melanogaster were expressed in Sf9 cells transfected with recombinant baculovirus. Resistance of L. cuprina to organophosphorus insecticides is due to mutations in the E3 gene that enhance the enzyme's ability to hydrolyse insecticides. Previous in vitro mutagenesis and expression of these modifications (G137D, in the oxyanion hole and W251L, in the acyl pocket) have confirmed their functional significance. We have systematically substituted these and nearby amino acids by others expected to affect the hydrolysis of pyrethroid insecticides. Most mutations of G137 markedly decreased pyrethroid hydrolysis. W251L was the most effective of five substitutions at this position. It increased activity with trans permethrin 10-fold, and the more insecticidal cis permethrin >130-fold, thereby decreasing the trans:cis hydrolysis ratio to only 2, compared with >25 in the wild-type enzyme. Other mutations near the bottom of the catalytic cleft generally enhanced pyrethroid hydrolysis, the most effective being F309L, also in the presumptive acyl binding pocket, which enhanced trans permethrin hydrolysis even more than W251L. In these assays with racemic 1RS cis and 1RS trans permethrin, two phases were apparent, one being much faster suggesting preferential hydrolysis of one enantiomer in each pair as found previously with other esterases. Complementary assays with individual enantiomers of deltamethrin and the dibromo analogue of cis permethrin showed that the wild type and most mutants showed a marked preference for the least insecticidal 1S configuration, but this was reversed by the F309L substitution. The W251L/F309L double mutant was best overall in hydrolysing the most insecticidal 1R cis isomers. The results are discussed in relation to likely steric effects on enzyme-substrate interactions, cross-resistance between pyrethroids and malathion, and the potential for bioremediation of pyrethroid residues.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","2009","Heymann, W. R.","Head lice treatments: Searching for the path of least resistance","","61(2):323-324","a6ec8591-e696-43c3-bd27-399ffc60607c","","Dialogues in Dermatology, a monthly audio program from the American Academy of Dermatology, contains discussions between dermatologists on timely topics. Commentaries from Dialogues Editor-in-Chief Warren R. Heymann, MD, are provided after each discussion as a topic summary and are provided here as a special service to readers of the Journal of the American Academy of Dermatology. Â© 2009 American Academy of Dermatology, Inc.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","2002","Horne, I., Sutherland, T. D., Harcourt, R. L., Russell, R. J., Oakeshott, J. G.","Identification of an opd (organophosphate degradation) gene in an Agrobacterium isolate","Applied and environmental microbiology","68(7):3371-6","631a353e-d429-4789-aa40-3e6b27f2916f","","We isolated a bacterial strain, Agrobacterium radiobacter P230, which can hydrolyze a wide range of organophosphate (OP) insecticides. A gene encoding a

protein involved in OP hydrolysis was cloned from A. radiobacter P230 and sequenced. This gene (called opdA) had sequence similarity to opd, a gene previously shown to encode an OP-hydrolyzing enzyme in Flavobacterium sp. strain ATCC 27551 and Brevundimonas diminuta MG. Insertional mutation of the opdA gene produced a strain lacking the ability to hydrolyze OPs, suggesting that this is the only gene encoding an OP-hydrolyzing enzyme in A. radiobacter P230. The OPH and OpdA proteins, encoded by opd and opdA, respectively, were overexpressed and purified as maltose-binding proteins, and the maltose-binding protein moiety was cleaved and removed. Neither protein was able to hydrolyze the aliphatic OP malathion. The kinetics of the two proteins for diethyl OPs were comparable. For dimethyl OPs, OpdA had a higher k(cat) than OPH. It was also capable of hydrolyzing the dimethyl OPs phosmet and fenthion, which were not hydrolyzed at detectable levels by OPH.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","2015","How, V., Hashim, Z., Ismail, P., Omar, D., Md Said, S., Tamrin, S. B. M.","Characterization of risk factors for DNA damage among paddy farm worker exposed to mixtures of organophosphates","","70(2):102-109","fb76a81e-dd77-4fef-95cb-003cd395c2be","","This is a cross-sectional study conducted among paddy farmers to characterize potential risk factors that influence levels of DNA damage from exposure to mixtures of organophosphates. Comet assay was used to determine the level of DNA damage by measuring the comet tail length from the exfoliated buccal mucosa. The result suggests that farmers who chronically exposure to a mixture of organophosphates has at least 2-fold significant increase of DNA damage as compared with control group. Factor analysis and linear regression both suggest that DNA damage reported by farmers may influence individual, occupational, and residential factors and are reported as significant predictor factors, whereas this effect is mainly caused by individual factors among the control group. The findings of the present study suggest that either farmer or control group bear certain extent of genotoxic burden contributed by different risk
factors.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","2011","Hunt, R. H., Fuseini, G., Knowles, S., Stiles-Ocran, J., Verster, R., Kaiser, M. L., Choi, K. S., Koekemoer, L. L., Coetzee, M.","Insecticide resistance in malaria vector mosquitoes at four localities in Ghana, West Africa","","4(1)","4d2648ec-a6ad-41eb-8e2a-6b6657317d8f","","Background: Malaria vector control programmes that rely on insecticide-based interventions such as indoor house spraying with residual insecticides or insecticide treated bed nets, need to base their decision-making process on sound baseline data. More and more commercial entities in Africa, such as mining companies, are realising the value to staff productivity of controlling malaria transmission in their areas of operation. This paper presents baseline entomological data obtained during surveys conducted for four mining operations in Ghana, West Africa. Results: The vast majority of the samples were identified as Anopheles gambiae S form with only a few M form specimens being identified from Tarkwa. Plasmodium falciparum infection rates ranged from 4.5 to 8.6% in An. gambiae and 1.81 to 8.06% in An. funestus. High survival rates on standard WHO bioassay tests were recorded for all insecticide classes except the organophosphates that showed reasonable mortality at all locations (i.e. > 90%). The West African kdr mutation was detected and showed high frequencies in all populations. Conclusions: The data highlight the complexity of the situation prevailing in southern Ghana and the challenges facing the malaria vector control programmes in this region. Vector control programmes in Ghana need to carefully

consider the resistance profiles of the local mosquito populations in order to base their resistance management strategies on sound scientific data. Â© 2011 Hunt et al; licensee BioMed Central Ltd.","","","RefMan","","","","","","","","","","Unknown","Unknown","Unknown","Unknown","","","2015","Hussien, N. A., Abd El-Azez, A. M., Hamza, R. Z.","Assessment of the genotoxic and mutagenic effect of al-taif pomegranate (Punica granatum L) peel extract alone and combined with malathion and atrazine pesticides in liver of male albino mice","","8(4):302-307","4ff4b141-5b56-4dcf-bfa6-99524bbec5ee","","In our previous studies, we report the antioxidant, hepatoprotective and nephroprotective potential of of Al-Taif Pomegranate (Punica granatum L) extracts against toxicity induced by Malathion (Mal) and Atrazine (Atra) pesticides in male albino mice. Hereby, we assess the genotoxic and mutagenic potential of Al-Taif Pomegranate (P. granatum L) peel extract (PPE) alone and combined with Atra and Mal pesticides in the liver of male albino mice. Our results report PPE genotoxicity and its failure to significantly decrease the genotoxic effect of the pesticides Mal and Atra. Genotoxic potential was reported by using Comet assay, in which fifty isolated comets were randomly selected and used to measure tail length, % DNA of tail and tail moment for each group in comparison with the negative control group. Moreover, PPE combined (Mal and Atra) groups show DNA point of mutation in P53 exon 5, that was detected by the highly sensitive and accurate assay single-strand conformation polymorphism (SSCP), represented by an extra third band in comparison with the negative control group. This mutation was not detected by direct sequencing, means that it is a low-frequency mutation. In conclusion, our results report Al-Taif PPE as a genotoxic extract and mutagenic in combination with Mal and Atra pesticides. Moreover, the present results also confirm the sensitivity of SSCP technique in detection of point of mutation in comparison to direct sequencing.","","","RefMan","","","","","","","","","","Unknown","Unknown","Unknown","Unknown","","","2014","Ibrahim, S. S., Manu, Y. A., Tukur, Z., Irving, H., Wondji, C. S.","High frequency of kdr L1014F is associated with pyrethroid resistance in Anopheles coluzzii in Sudan savannah of northern Nigeria","BMC infectious diseases","14:441","1396c461-d54d-4326-bdd1-bd149f863f65","","BACKGROUND: Malaria burden is high in Nigeria, yet information on the major mosquito vectors is lacking especially in the Sudan savannah region of the country. In order to facilitate the design of future insecticide-based control interventions in the region, this study has established the resistance profile of An. gambiae s.l. populations in two northern Nigeria locations and assessed the contribution of target site resistance mutations. METHODS: Larval collection was conducted in two localities in Sudan savannah (Bunkure and Auyo) of northern Nigeria between 2009 and 2011, from which resulting adult, female mosquitoes were used for insecticides bioassays with deltamethrin, lambda-cyhalothrin, DDT and malathion. The mosquitoes were identified to species level and molecular forms and then genotyped for the presence of L1014F-kdr, L1014S-kdr and ace-1R mutations. RESULTS: WHO bioassays revealed that An. gambiae s.l. from both localities were highly resistant to lambda-cyhalothrin and DDT, but only moderately resistant to deltamethrin. Full susceptibility was observed to malathion. An. gambiae, M form (now An. coluzzii), was predominant over An. arabiensis in Auyo and was more resistant to lambda-cyhalothrin than An. arabiensis. No 'S' form (An. gambiae s.s.) was detected. A high frequency of 1014 F mutation (80.1%) was found in An. coluzzii in contrast to An. arabiensis (13.5%). The presence of the 1014 F kdr allele was significantly associated with resistance to lambda-cyhalothrin in An. coluzzii (OR = 9.85; P < 0.001) but not in

An. arabiensis. The L1014S-kdr mutation was detected in a single An. arabiensis mosquito while no ace-1R mutation was found in any of the mosquitoes analysed. CONCLUSIONS: The predominance of An. coluzzii and its resistance profile to main insecticides described in this study can guide the implementation of appropriate vector control interventions in this region of Nigeria where such information was previously lacking.","","","RefMan","","","","","","","","","",""
"Unknown","Unknown","Unknown","Unknown","","","2015","Ishak, I. H., Jaal, Z., Ranson, H., Wondji, C. S.","Contrasting patterns of insecticide resistance and knockdown resistance (kdr) in the dengue vectors Aedes aegypti and Aedes albopictus from Malaysia","Parasites & vectors","8:181","aa5d5d1f-cb9f-41b9-aa54-9fa7f4083c94","","BACKGROUND: Knowledge on the extent, distribution and mechanisms of insecticide resistance is essential for successful insecticide-based dengue control interventions. Here, we report an extensive resistance profiling of the dengue vectors Aedes aegypti and Aedes albopictus across Malaysia and establish the contribution of knockdown resistance mechanism revealing significant contrast between both species. METHODS: Aedes mosquitoes were collected from four states in Malaysia in 2010 using ovitraps and tested against six major insecticides using WHO bioassays. Knockdown resistance (kdr) was investigated in both species. RESULTS: A moderate resistance to temephos was detected from samples collected in 2010 in Penang, Kuala Lumpur, Johor Bharu and Kota Bharu (1.5 < RR < 3.3). A widespread and multiple resistances was observed in Ae. aegypti particularly against pyrethroids, DDT and bendiocarb. Mosquitoes from Kuala Lumpur consistently had the highest resistance levels and was the only population showing a moderate resistance to malathion (91% mortality). The resistance profile of Ae. albopictus contrasted to Ae. aegypti with full susceptibility to pyrethroids except in Kuala Lumpur where moderate resistance is observed. PBO synergist assays suggest metabolic resistance mechanisms play a major role in resistance in both species. Two kdr mutations, F1534C and V1016G, were detected in Ae. aegypti across Malaysia but neither of these mutations were found in Ae. albopictus. Additionally, signatures of selection were detected on the Voltage-gated sodium channel gene in Ae. aegypti but not in Ae. albopictus. The presence of the 1534C allele was significantly associated with pyrethroid resistance and an additive effect to pyrethroid resistance was observed in individuals containing both kdr alleles. CONCLUSIONS: Findings from this study will help to design and implement successful insecticide-based interventions against Ae. aegypti and Ae. albopictus to improve dengue control across Malaysia.","","","RefMan","","","","","","","","","",""
"Unknown","Unknown","Unknown","Unknown","","","2012","Jira, D., Janousek, S., Pikula, J., Vitula, F., Kejlova, K.","Toxicity hazard of organophosphate insecticide malathion identified by in vitro methods","Neuro endocrinology letters","33 Suppl 3:53-9","9520fdea-27ea-46e0-94a8-b2a68253cc34","","OBJECTIVES: Malathion is generally not classified as toxic. However, the toxicity seems to be species-dependent. Local and systemic toxicity data for birds are rare, but a decrease of wild bird densities in areas where malathion was applied was reported. Aim of the study was to extend knowledge on malathion toxicity on cellular and organ level and to evaluate embryotoxicity and genotoxicity for birds using the chick embryo model HET-CAM. METHODS: Skin and eye irritation was determined using reconstructed skin and eye cornea tissues and the chorioallantoic membrane of chick embryo to simulate conjunctiva. Cytotoxicity in 3T3 Balb/c fibroblast culture was determined to estimate acute systemic toxicity. Chick embryo model was further employed to evaluate acute embryotoxicity for

birds (mortality and genotoxicity). Data were analysed by means of general linear models. RESULTS: Malathion is not a skin and eye irritant. Cytotoxicity in vitro test provided LD50 value of 616 mg/kg suggesting higher toxic potential than is generally published based on in vivo tests on laboratory rodents. Embryotoxicity studies revealed dose and age dependent mortality of chick embryos. Genotoxicity was identified by means of micronucleus test in erythroid cells isolated from chorioallantois vascular system of chick embryos. CONCLUSIONS: Using in vitro alternative toxicological methods, a higher toxic potential of malathion was demonstrated than is generally declared. An increased health and environmental hazard may occur in areas with intensive agricultural production. The environmental consequences of delayed effects and embryotoxicity for bird populations in areas exposed to organophosphate insecticides, such as malathion, are obvious.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","2012","Jira, D., Kejlova, K., Janousek, S., Pikula, J., Vitula, F.","Local toxicity and embryotoxicity of organophosphate insecticide (malathion) identified by alternative in vitro methods","","40(4):A41","1cb830f2-ccfa-43d8-8b01-9951237d2e7d","","The organophosphate insecticide, Malathion, is reported to be of low toxicity for man. Based on a LD50 value over 2000mg/kg for the rat and the mouse, it is generally not classified as toxic. The toxicity seems to be species-dependent, and is particularly dependent on carboxylesterase activity that breaks down toxic malaoxon generated in the liver by cytochrome P450. Distinct data also suggest inhibition of the thyroid gland hormones, degeneration of ovary follicle cells and increase in the incidence of fetus resorption. Local and systemic toxicity data for birds are rare and/or ambiguous, but a decrease in wild bird densities in areas where malathion was applied is repeatedly reported. The actual intoxication of wild birds may be influenced by the level of exposure from multiple sources, by age and sex of animals, by their state of nutrition and body condition. With the aim of extending knowledge on Malathion toxicity at the cellular and organ levels, we performed a number of experiments with progressive alternative in vitro methods that model local and systemic toxicity. The cytotoxicity was assessed in 3T3 fibroblast cultures. Skin and eye irritation potential was determined by using reconstructed skin and eye cornea tissues (EpiDermâ„¢ and EpiOcularâ„¢). As no skin and eye cornea irritation potential was demonstrated, the HET-CAM test, which utilises the rich vascular system of the chorioallantoic membrane of chicken embryos in fertilised hen eggs, was used to detect effects on mucosa. The chick embryo model was employed further for an extended study on acute embryotoxicity (mortality and genotoxicity), dependent on the time and place of Malathion intra-embryonal application up to day 8 of chick embryo development. If Malathion was applied into the amnion cavity, then chick embryo mortality was identified at lower doses, at higher incidence and in earlier stages of development, in comparison with application into the air cavity. No genotoxicity was identified by means of the micronucleus test in erythroid MNE I and MNE II cells isolated from the chick embryo chorioallantoic vascular system, following morphological evaluation by optical and fluorescent microscopy. No significant changes in micronucleus and mitosis numbers were detected. The IC50 of 54.2 Â± 3.1Î¼g/ml, obtained by using the in vitro cytotoxicity test, which was recently validated as suitable to identify non-toxic, i.e. not classified, substances, suggests higher toxic potential of Malathion than is generally declared in literature based on conventional in vivo tests on laboratory rodents.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","2011","Jose, S., Jayesh, P., Mohandas,

A., Philip, R., Bright Singh, I. S.","Application of primary haemocyte culture of Penaeus monodon in the assessment of cytotoxicity and genotoxicity of heavy metals and pesticides","Marine environmental research","71(3):169-77","279eeabd-e11b-402e-bf55-f8b535d47f3c","","Lack of shrimp cell lines has hindered the study of pollutants which adversely affects shrimp health and its export value. In this context a primary haemocyte culture developed from Penaeus monodon was employed for assessing the cytotoxicity and genotoxicity of two heavy metal compounds, cadmium chloride and mercuric chloride and two organophosphate insecticides, malathion and monocrotophos. Using MTT assay 12 h IC(50) values calculated were 31.09 +/- 16.27 muM and 5.52 +/- 1.16 muM for cadmium chloride and mercuric chloride and 59.94 +/- 52.30 mg l(-1) and 186.76 +/- 77.00 mg l(-1) for malathion and monocrotophos respectively. Employing Comet assay, DNA damage inflicted by these pollutants on haemocytes were evaluated and the pollutants induced DNA damage in >60% of the cells. The study suggested that haemocyte culture could be used as a tool for quantifying cytotoxicity and genotoxicity of aquaculture drugs, management chemicals and pollutants.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","2014","Josse, R., Sharanek, A., Savary, C. C., Guillouzo, A.","Impact of isomalathion on malathion cytotoxicity and genotoxicity in human HepaRG cells","Chemico-biological interactions","209:68-76","bc6369ce-5fc0-47a8-823b-a3b0b04e7baa","","Isomalathion is a major impurity of technical grade malathion, one of the most abundantly applied insecticides; however little is known about its hepatotoxicity. In the present study, cytotoxicity and genotoxicity of malathion and isomalathion either individually or in combination, were assessed using the metabolically competent human liver HepaRG cell line. Isomalathion reduced cell viability starting at a 100 muM concentration after a 24h exposure. It also significantly induced caspase-3 activity in a dose-dependent manner starting at 5 muM. On the contrary, even at concentrations as high as 500 muM malathion affected neither cell viability nor caspase-3 activity. Moreover, co-exposure of both compounds resulted in decreased toxicity of isomalathion. By contrast, malathion and isomalathion either separately or in combination, slightly induced micronuclei formation at low concentrations and had additive genotoxic effects when combined at 25 muM. Individually or combined isomalathion directly inhibited activity of carboxyesterases which are involved in detoxication of malathion. In addition, transcripts of CYP2B6 and CYP3A4, two CYPs responsible for malathion phase I metabolism, were strongly induced by the mixture while isomalathion alone only moderately decreased CYP1A2 and increased CYP2B6 transcripts. However, these CYPs were not altered at the protein or activity levels. Taken altogether, our results showed that isomalathion was much more cytotoxic than malathion while both compounds had comparable genotoxic effects in HepaRG hepatocytes at low concentrations and brought further support to the importance of considering impurities and interactions during evaluation of health risks of pesticides.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","2016","Jyoti, Singh, N. K., Singh, H., Singh, N. K., Rath, S. S.","Multiple mutations in the acetylcholinesterase 3 gene associated with organophosphate resistance in Rhipicephalus (Boophilus) microplus ticks from Punjab, India","Veterinary parasitology","216:108-17","49f6e525-425d-48ec-8305-2ea32597772d","","The organophosphate (OP) resistance status in Rhipicephalus (Boophilus) microplus ticks collected from seventeen districts located in the northwestern Indian state, Punjab were characterized using three data sets (bioassay,

biochemical and molecular assays). Adult immersion test (AIT) was adopted and the resistance factors (RF) for the field isolates were determined. Resistance to malathion was detected in 12 isolates among which 11 showed level I resistance status while level II status was recorded in one isolate (RF of 5.35). To understand the possible mechanism of resistance development, acetylcholinesterase (AChE) activity and gene sequences of the AChE3 were analyzed. A significantly (P<0.001) higher level of percent uninhibited AChE activity was recorded in all field isolates (36.36+/-0.46-43.77+/-1.21) in comparison to the susceptible population (29.39+/-0.40). The AChE activity was positively correlated with RF against malathion with a correlation coefficient (r) of 0.359. Analysis of nucleotides and their deduced amino acids sequences of partial AChE3 gene revealed the presence of six amino acid substitutions (I48L, I54V, V71A, I77M, S79P and R86Q). Three novel amino acid substitutions (V71A, I77M and S79P) in partial AChE3 gene were also identified in some of the isolates which may possibly have a role in OP resistance development. The PCR-RFLP assay with HaeIII revealed the presence of restriction site corresponding to R86Q mutation in all the field isolates along with an additional restriction site in seven field isolates corresponding to V71A mutation. The results of the study indicate the involvement of both insensitive AChE and higher percent uninhibited AChE activity as the possible mechanism in these field isolates.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","2014","Kandiel, M. M., El-Asely, A. M., Radwan, H. A., Abbass, A. A.","Modulation of genotoxicity and endocrine disruptive effects of malathion by dietary honeybee pollen and propolis in Nile tilapia (Oreochromis niloticus)","Journal of advanced research","5(6):671-84","9e6d4a0e-320f-4196-a39d-3f9d86cd352d","","The present study aimed at verifying the usefulness of dietary 2.5% bee-pollen (BP) or propolis (PROP) to overcome the genotoxic and endocrine disruptive effects of malathion polluted water in Oreochromis niloticus (O. niloticus). The acute toxicity test was conducted in O. niloticus in various concentrations (0-8 ppm); mortality rate was assessed daily for 96 h. The 96 h-LC50 was 5 ppm and therefore 1/5 of the median lethal concentration (1 ppm) was used for chronic toxicity assessment. In experiment (1), fish (n = 8/group) were kept on a diet (BP/PROP or without additive (control)) and exposed daily to malathion in water at concentration of 5 ppm for 96 h ""acute toxicity experiment"". Protective efficiency against the malathion was verified through chromosomal aberrations (CA), micronucleus (MN) and DNA-fragmentation assessment. Survival rate in control, BP and PROP groups was 37.5%, 50.0% and 100.0%, respectively. Fish in BP and PROP groups showed a significant (P < 0.05) reduction in the frequency of CA (57.14% and 40.66%), MN (53.13% and 40.63%) and DNA-fragmentation (53.08% and 30.00%). In experiment (2), fish (10 males and 5 females/group) were kept on a diet with/without BP for 21 days before malathion-exposure in water at concentration of 0 ppm (control) or 1 ppm (Exposed) for further 10 days ""chronic toxicity experiment"". BP significantly (P < 0.05) reduced CA (86.33%), MN (82.22%) and DNA-fragmentation (93.11%), prolonged the sperm motility when exposed to 0.01 ppm of pollutant in vitro and increased the estradiol level in females comparing to control. In conclusion, BP can be used as a feed additive for fish prone to be raised in integrated fish farms or cage culture due to its potency to chemo-protect against genotoxicity and sperm-teratogenicity persuaded by malathion-exposure.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","2008","Kapoli, P., Axarli, I. A., Platis, D., Fragoulaki, M., Paine, M., Hemingway, J., Vontas, J., Labrou, N.

E.","Engineering sensitive glutathione transferase for the detection of xenobiotics","Biosensors & bioelectronics","24(3):498-503","03a889f2-bb6a-4fe0-89fa-fd79af43a0a4","","Cytosolic glutathione transferases (GSTs) are a major reserve of high-capacity ligand binding proteins which recognise a large variety of hydrophobic compounds. In the present study, the binding of non-substrate xenobiotic compounds (herbicides and insecticides) to maize GST I was investigated by employing kinetic inhibition studies, site-directed mutagenesis and molecular modelling studies. The results showed that the xenobiotics bind at the substrate binding site. Based on in silico docking analysis, two residues were selected for assessing their contribution to xenobiotic binding. The mutant Gln53Ala of GST I Exhibits 9.2-fold higher inhibition potency for the insecticide malathion, compared to the wild-type enzyme. A potentiometric assay was developed for the determination of malathion using the Gln53Ala mutant enzyme. The assay explores the ability of the xenobiotic to promote inhibition of the GST-catalysing 1-chloro-2,4-dinitrobenzene (CDNB)/glutathione (GSH) conjugation reaction. The sensing scheme is based on the pH change occurring in a low buffer system by the GST reaction, which is measured potentiometrically using a pH electrode. Calibration curve was obtained for malathion, with useful concentration range 0-20 microM. The method's reproducibility was in the order of +/-3-5% and malathion recoveries were 96.7+/-2.8%. Immobilized Gln53Ala mutant GST was used to assemble a biosensor for malathion. The enzyme was immobilized by crosslinking with glutaraldehyde and trapped behind a semipermeable membrane in front of the pH electrode. The results demonstrated that the immobilized enzyme behaved similar to free enzyme.","","","RefMan","","","","","","","","",""
"Unknown","Unknown","Unknown","Unknown","","","2013","KarabaÊ‡ Ã‡oban, F., Ince, S., KÃ¼cÂ¸Ã¼kkurt, I., Hazman, Ã-, Demirel, H. H.","The effects of boron on malathion toxicity","","38","c59969ae-3873-49dd-9c18-79b945c9b00f","","Objective: In this study, effects of boron on acitivities of malondialdehyde (MDA), reduced glutathione (GSH) and nitric oxide (NO), superoxide dismutase (SOD), catalase (CAT) in brain, kidney, liver and serum acetylcholinesterase (AChE), 8 hydroxy guanine (8ohG) in malathion toxicity with rats Material and Methods: A total of 48 mature male Wistar albino rats were randomly divided into 6 groups of 8 including. AChE and 8-OHdG in serum and brain tissue levels were determined by ELISA. Histopathological evaluations were performed in various tissues. Pesticide residues in tissues were examined by ICP-MS. Antioxidants and reactive oxygen parameters were determined by spectrophotometric method. Statistical analysis was performed using the SPSS 18 program. Results: Malthion inhibited AChE activity, a marker of oxidative DNA damage 8-ohG levels were significantly (p <0.005) increased.T issue and serum MDA levels were significantly increased (p <0.005) and antioxidant parameters were significantly decreased (p <0.005). Malathion tissue samples of the groups results in hepatocytes, degeneration and necrosis, dejenarasyon tubular epithelial cells, brain cells were neuronophagia. Boron, the damage created by malathion showed a therapeutic effect. Conclusion: As a result, malathion which primarily inhibits acetylcholinesterase (AChE) activity in the nervous system causes significant (p<0.05) however which is as a result of oxidative DNA damage causing increased levels of 8 hydroxy guanine. Malathion observed that oxidative stress. Boron has shown positive effects against these toxic effects.","","","RefMan","","","","","","","","","",""
"Unknown","Unknown","Unknown","Unknown","","","2014","Karami-Mohajeri, S., Hadian, M. R., Fouladdel, S., Azizi, E., Ghahramani, M. H., Hosseini, R., Abdollahi,

M.","Mechanisms of muscular electrophysiological and mitochondrial dysfunction following exposure to malathion, an organophosphorus pesticide","Human & experimental toxicology","33(3):251-63","86a4fa3d-d4b1-45e2-9823-5ecee33f257f","","Muscle dysfunction in acute organophosphorus (OP) poisoning is a cause of death in human. The present study was conducted to identify the mechanism of action of OP in terms of muscle mitochondrial dysfunction. Electromyography (EMG) was conducted on rats exposed to the acute oral dose of malathion (400 mg/kg) that could inhibit acetylcholinesterase activity up to 70%. The function of mitochondrial respiratory chain and the rate of production of reactive oxygen species (ROS) from intact mitochondria were measured. The bioenergetic pathways were studied by measurement of adenosine triphosphate (ATP), lactate, and glycogen. To identify mitochondrial-dependent apoptotic pathways, the messenger RNA (mRNA) expression of bax and bcl-2, protein expression of caspase-9, mitochondrial cytochrome c release, and DNA damage were measured. The EMG confirmed muscle weakness. The reduction in activity of mitochondrial complexes and muscular glycogen with an elevation of lactate was in association with impairment of cellular respiration. The reduction in mitochondrial proapoptotic stimuli is indicative of autophagic process inducing cytoprotective effects in the early stage of stress. Downregulation of apoptotic signaling may be due to reduction in ATP and ROS, and genotoxic potential of malathion. The maintenance of mitochondrial integrity by means of artificial electron donors and increasing exogenous ATP might prevent toxicity of OPs.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","2008","Kerah-Hinzoumbe, C., Peka, M., Nwane, P., Donan-Gouni, I., Etang, J., Same-Ekobo, A., Simard, F.","Insecticide resistance in Anopheles gambiae from south-western Chad, Central Africa","Malaria journal","7:192","1ff1a4c3-3475-4aab-bf91-fc15aca123a2","","BACKGROUND: Indoor residual spraying and insecticide-treated nets (ITN) are essential components of malaria vector control in Africa. Pyrethroids are the only recommended compounds for nets treatment because they are fast-acting insecticides with low mammalian toxicity. However, there is growing concern that pyrethroid resistance may threaten the sustainability of ITN scaling-up programmes. Here, insecticide susceptibility was investigated in Anopheles gambiae sensu lato from an area of large scale ITN distribution programme in south-western Chad. METHODS: Susceptibility to 4% DDT, 0.05% deltamethrin, 0.75% permethrin, 0.1% bendiocarb and 5% malathion was assessed using the WHO standard procedures for adult mosquitoes. Tests were carried out with two to four days-old, non-engorged female mosquitoes. The An. gambiae Kisumu strain was used as a reference. Knockdown effect was recorded every 5 min and mortality scored 24 h after exposure. Mosquitoes were identified to species and molecular form by PCR-RFLP and genotypes at the kdr locus were determined in surviving specimens by Hot Oligonucleotide Ligation Assay (HOLA). RESULTS: During this survey, full susceptibility to malathion was recorded in all samples. Reduced susceptibility to bendiocarb (mortality rate of 96.1%) was found in one sample out of nine assayed. Increased tolerance to pyrethroids was detected in most samples (8/9) with mortality rates ranging from 70.2 to 96.6% for deltamethrin and from 26.7 to 96.3% for permethrin. Pyrethroid tolerance was not associated with a significant increase of knock-down times. Anopheles arabiensis was the predominant species of the An. gambiae complex in the study area, representing 75 to 100% of the samples. Screening for kdr mutations detected the L1014F mutation in 88.6% (N = 35) of surviving An. gambiae sensu stricto S form mosquitoes. All surviving An. arabiensis (N = 49) and M form An. gambiae s.s. (N = 1) carried the susceptible allele. CONCLUSION:

This first investigation of malaria vector susceptibility to insecticides in Chad revealed variable levels of resistance to pyrethroid insecticides (permethrin and deltamethrin) in most An. gambiae s.l. populations. Resistance was associated with the L1014F kdr mutation in the S form of An. gambiae s.s.. Alternative mechanisms, probably of metabolic origin are involved in An. arabiensis. These results emphasize the crucial need for insecticide resistance monitoring and in-depth investigation of resistance mechanisms in malaria vectors in Chad. The impact of reduced susceptibility to pyrethroids on ITN efficacy should be further assessed.","","","RefMan","","","","","","","","","","Unknown","Unknown","Unknown","Unknown","","","2011","Koekemoer, L. L., Spillings, B. L., Christian, R. N., Lo, T. C. M., Kaiser, M. L., Norton, R. A. I., Oliver, S. V., Choi, K. S., Brooke, B. D., Hunt, R. H., Coetzee, M.","Multiple insecticide resistance in Anopheles gambiae (Diptera: Culicidae) from Pointe Noire, Republic of the Congo","","11(8):1193-1200","f4e2f9e8-ee87-4b67-9346-36c3b90b42da","","Successful implementation of an integrated vector control program will rely on availability of accurate vector information in the specific location. However, such information can be limited in some countries. The aim of this study was to obtain baseline vector information from Pointe Noire on the Congo coast (Republic of the Congo). Field sampling was conducted during April 2009 in the village of Boutoto and its surrounds, close to the city of Pointe Noire. Anopheles gambiae sensu lato mosquitoes were collected resting indoors. Samples were analyzed for insecticide susceptibility, species identification, and Plasmodium sporozoite infection. Molecular and biochemical assays were conducted to characterize insecticide resistance mechanisms. The malaria vector A. gambiae S-form was the only mosquito species identified, and it had a high Plasmodium falciparum infection rate (9.6%). Multiple insecticide resistance was detected in this population with full susceptibility to only one insecticide class, the organophosphates. Dieldrin and DDT resistance was mainly attributed to target-site resistance (the Rdl and L1014F/L1014S kdr mutations respectively), whereas pyrethroid resistance was mainly attributed to P450 metabolic enzyme-mediated detoxification in addition to kdr. The role of various insecticide resistance mechanisms revealed a complex association between metabolic detoxification and reduced target-site sensitivity. Â© Copyright 2011, Mary Ann Liebert, Inc.","","","RefMan","","","","","","","","","","Unknown","Unknown","Unknown","Unknown","","","2006","Kristensen, M., Knorr, M., Rasmussen, A. M., Jespersen, J. B.","Survey of permethrin and malathion resistance in human head lice populations from Denmark","Journal of medical entomology","43(3):533-8","c9e9a1bb-52cc-4767-9477-976e756cf8de","","Head lice, Pediculis capitis De Geer, populations were investigated for permethrin and malathion resistance after initial establishment of a discriminating dose of topical application bioassay with body lice, Pediculus humanus L. For both insecticides, approximately 2 times the lethal dose (LD)95 at 4 h was selected, 2 ng of permethrin and 100 ng of malathion per head louse, respectively. Head lice were collected from heads of infested children in Denmark at 33 primary schools, one kindergarten, and seven boarding schools. The lice were collected by combing of dry hair, with a fine-toothed antilouse comb attached to a vacuum cleaner. A resistance survey covers head lice collected from 208 of 1,441 persons combed. The frequency of permethrin- and malathion-resistant head lice is high in Danish head lice populations. In 17 of 24 samples tested for permethrin resistance, all head lice survived the discriminating dose. Six samples had between 3 and 25% dead head

lice, whereas one sample had 60% mortality. In nine of 25 samples tested for malathion resistance, all head lice survived the discriminating dose. Seven samples had <25% dead head lice, and four samples had a mortality of 50% or more at the discriminating dose. The connection between permethrin resistance and kdr-like mutations is confirmed by our findings. The frequency of the double mutation T929I-L932 F in the voltage-sensitive sodium channel gene associated with permethrin resistance was 0.95 in Danish head lice populations.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","2015","Kudom, A. A., Mensah, B. A., Froeschl, G., Boakye, D., Rinder, H.","Preliminary assessment of the potential role of urbanization in the distribution of carbamate and organophosphate resistant populations of Culex species in Ghana","Parasites & vectors","8:8","692877b4-1f21-4622-976b-c6c80d7d60fb","","BACKGROUND: Besides its role as a pathogen vector, Culex species also indirectly promotes the transmission of malaria if the use of bed nets or indoor residual spraying is discontinued due to a lack of insecticide efficacy against it. A recent survey revealed widespread occurrence of pyrethroid resistance among urban populations of this mosquito in Ghana. In order to plan and implement insecticide-based resistance management strategies, this study was carried out to assess resistance status of Culex species to organophosphate and carbamate in urban areas in Ghana and the possible mechanisms involved as well as environmental factors associated with its distribution. METHODS: Mosquito larvae were sampled from various land use and ecological settings and in different seasons. In adults, susceptibility to organophosphates (fenitrothion, malathion) and carbamates (propoxur, bendiocarb) were determined. Mixed function oxidase (MFO) and alpha- and beta-esterase assays, as well as a PCR diagnostic assay to determine ace1 mutation were performed in individual mosquitoes. RESULTS: Culex quinquefasciatus as well as C. decens and other unidentified Culex species were found breeding in polluted water bodies in the study sites. Across all sites and seasons, carbamate induced mortality was 94.1% +/- 15.4 whereas mortality caused by organophosphate was 99.5% +/- 2.2. In addition, ace1 mutation and high levels of esterases were detected in some of the mosquito populations. There was a strong correlation between susceptibility status of the mosquitoes and the level of absorbance of beta-esterase (Pearson r=- 0.841, p=0.004). CONCLUSIONS: The study found low prevalence of resistance to carbamate and organophosphate insecticides among Culex species from Ghana. However, there were populations with ace1 mutations and high levels of esterases, which can confer high resistance to these classes of insecticides. Thus, it is important to monitor activities or behaviour that has the potential to select for carbamate and organophosphate resistance
populations.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","1995","Kumar, D., Khan, P. K., Sinha, S. P.","Cytogenetic toxicity and no-effect limit dose of pesticides","Food and chemical toxicology : an international journal published for the British Industrial Biological Research Association","33(4):309-14","d0aba846-e997-4872-a121-f286bc3ad5b2","","The no-effect limit dose (NELD) of three commonly used pesticides with respect to their cytogenetic toxicity was determined in a number of test systems using a sufficient number of lower doses to characterize the dose-effect relationship. For lindane, malathion and metacid, this dose was 3.2, 7.0 and 3.0 mg/litre, respectively, for mitosis inhibition and 9.0, 55 and 60 mg/litre, respectively, for chromosome clastogeny in onion root-tip cells. For chromosome clastogeny in mice bone marrow cells, the NELDs of the three pesticides were 1.6, 1.5 and 2.0 mg/kg body weight/day, respectively.

These values for dominant lethals and X-chromosome-linked recessive lethals in Drosophila were 20 and 5 micrograms lindane/litre, 2 and 3.5 micrograms malathion/litre and 4 and 5.5 micrograms metacid/litre, respectively. Thus, the NELDs are not only pesticide specific but also organism specific, tissue specific and even damage specific. Furthermore, the NELD values determined are so small that the real human exposure to pesticides cannot be reduced below these levels without compromising the effectiveness of pesticides in use.","","","RefMan","","","","","","","","","","Unknown","Unknown","Unknown","Unknown","","","2015","Kumar, N., Yadav, A., Gulati, S., Kanupriya, Aggarwal, N., Gupta, R.","Antigenotoxic potential of curcumin and carvacrol against malathion-induced DNA damage in cultured human peripheral blood and its relation to GSTM1 and GSTT1 polymorphism","","7(3):98-104","616e1582-0b11-40a8-baca-4b8a65dfe8c1","","The aerial application of malathion, a widely used organophosphate insecticide, has raised public concerns about its potential adverse health effects. We, therefore, studied the antigenotoxic potential of curcumin and carvacrol against malathion-induced DNA damage using sister chromatid exchange (SCE) as a biomarker of genotoxicity. To observe the antigenotoxic potential of curcumin and carvacrol, heparinized fresh blood from healthy individuals was treated with 30 Î¼g/mL of malathion in the presence of curcumin and carvacrol. Curcumin at concentrations of 25 Î¼g/mL and 50 Î¼g/mL had significantly reduced ($p < 0.05$) the frequency of SCE as compared to malathion-exposed sample. Similarly, carvacrol showed significant ($p < 0.05$) antigenotoxic effect at concentrations of 2.5 Î¼g/mL and 5.0 Î¼g/mL against malathion. We also studied the effect of GSTT1 and GSTM1 on the genotoxicity of malathion and antigenotoxic potential of curcumin and carvacrol. We observed that there is a statistically significant ($p < 0.05$) reduction in the frequency of SCE in case of curcumin and carvacrol as compared to malathion, but we did not observe any significant relationship ($p > 0.05$) between GSTT1 and GSTM1 polymorphism and the genotoxicity of malathion and antigenotoxic potential of curcumin and carvacrol.","","","RefMan","","","","","","","","","","Unknown","Unknown","Unknown","Unknown","","","2010","Kumar, R., Nagpure, N. S., Kushwaha, B., Srivastava, S. K., Lakra, W. S.","Investigation of the genotoxicity of malathion to freshwater teleost fish Channa punctatus (Bloch) using the micronucleus test and comet assay","Archives of environmental contamination and toxicology","58(1):123-30","af6023ea-1f60-448b-90cf-75029eba18e3","","Malathion [S-(1,2-dicarboethoxyethyl) O, O-dimethyl phosphorodithioate] is a widely used organophosphorus insecticide throughout the world. However, limited efforts have made to study its genotoxic effect in different fish tissues. The present investigation was aimed to assess the genotoxic potential of the pesticide to the freshwater teleost fish Channa punctatus at sublethal concentrations using the micronucleus test and comet assay. Initially, the 96-h LC50 value of commercial-grade malathion (50% EC) was determined as 5.93 ppm in a semistatic system. Based on LC50, three test concentrations (viz. sublethal I, sublethal II, and sublethal III) were determined to be 1.48, 0.74, and 0.59 ppm, respectively, and the fish specimens were exposed to these concentrations. Tissue samplings were done on days 0, 1, 3, 7, 15, 22 and 29 of malathion exposure for assessment of the induction of micronuclei (MN) frequency and DNA damage. The MN formation in the peripheral blood cells was found to be significantly higher ($p < 0.05$) in the treated specimens at all sampling intervals compared to the control. The MN frequency reached maximum on days 3 and 7 at sublethal I and II concentrations, respectively, followed by a nonlinear decline with the

progression of the experiment. Similarly, significant effects ($p < 0.05$) of both concentration and time of exposure were observed on DNA damage in the gill, kidney, and lymphocytes. All of the tissues exhibited a concentration-dependent increase in DNA damage up to day 3, followed by a nonlinear decrease with the duration of exposure. A comparison of the extent of DNA damage among the tissues showed the sensitivity of gill tissue to malathion.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","2014","Kwon, D. H., Kim, J. H., Kim, Y. H., Yoon, K. S., Clark, J. M., Lee, S. H.","Identification and characterization of an esterase involved in malathion resistance in the head louse Pediculus humanus capitis","Pesticide biochemistry and physiology","112:13-8","4f4f4575-87fa-4aa1-a24e-5a05066463f9","","Enhanced malathion carboxylesterase (MCE) activity was previously reported to be involved in malathion resistance in the head louse Pediculus humanus capitis (Gao et al., 2006 [8]). To identify MCE, the transcriptional profiles of all five esterases that had been annotated to be catalytically active were determined and compared between the malathion-resistant (BR-HL) and malathion-susceptible (KR-HL) strains of head lice. An esterase gene, designated HLCbE3, exhibited approximately 5.4-fold higher transcription levels, whereas remaining four esterases did not exhibit a significant increase in their transcription in BR-HL, indicating that HLCbE3 may be the putative MCE. Comparison of the entire cDNA sequences of HLCbE3 revealed no sequence differences between the BR-HL and KR-HL strains and suggested that no single nucleotide polymorphism is associated with enhanced MCE activity. Two copies of the HLCbE3 gene were observed in BR-HL, implying that the over-transcription of HLCbE3 is due to the combination of a gene duplication and up-regulated transcription. Knockdown of HLCbE3 expression by RNA interference in the BR-HL strain led to increases in malathion susceptibility, confirming the identity of HLCbE3 as a MCE responsible for malathion resistance in the head louse. Phylogenetic analysis suggested that HLCbE3 is a typical dietary esterase and belongs to a clade containing various MCEs involved in malathion resistance.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","2012","Lang, G. J., Zhu, K. Y., Zhang, C. X.","Can acetylcholinesterase serve as a target for developing more selective insecticides?","","13(4):495-501","f568b2bc-0d55-47f8-b9e5-51893c1f09bb","","Acetylcholinesterase (AChE; EC 3.1.1.7) is a primary target of many insecticides including organophosphates (OP) and carbamates (CB). Because AChE is expressed in all invertebrate and vertebrate animals as a key enzyme of the cholinergic system, the toxicity of anticholinesterase insecticides to mammals and non-target species such as beneficial insects has been a great concern. In addition, the intensive use of OP and CB insecticides has resulted in the development of resistance in many insect pests, which has limited the use of anticholinesterase insecticides. Many aces encoding AChEs have been sequenced from a variety of vertebrates, insects and other invertebrates, and crystal structures of four AChEs have been determined in the past 20 years. Although the primary motifs and the three dimensional (3D) structures of different AChEs are similar, differences among AChEs are obvious. The catalytic properties and inhibition kinetics of AChEs from different groups of insects and mammals may be quite different, and two AChEs from a single insect may also show distinct differences. These differences may provide new opportunities for designing more selective insecticides for pest management. Â© 2012 Bentham Science Publishers.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","2014","Lasram, M. M., Dhouib, I. B.,

Bouzid, K., Lamine, A. J., Annabi, A., Belhadjhmida, N., Ahmed, M. B., Fazaa, S. E., Abdelmoula, J., Gharbi, N.","Association of inflammatory response and oxidative injury in the pathogenesis of liver steatosis and insulin resistance following subchronic exposure to malathion in rats","Environmental toxicology and pharmacology","38(2):542-53","8333e774-3537-488c-a833-750e2a62262b","","Insulin resistance and risk of type 2 diabetes are the most important complications following exposure to organophosphorous (OPs) pesticides. Regarding the importance of liver on metabolic pathways regulation, in particular blood glucose homeostasis, we focused on liver inflammation and oxidative damages in a subchronic model of toxicity by malathion. Adult male Wistar rats of body weight 200-250g were used for the study. Malathion (200mg/kg b.w./day) was administered to rats by oral intubation for 28 days. Glycemic and insulin resistance indices, markers of liver injury, markers of inflammation and oxidative stress were assessed. Malathion-treated rats showed increased glycemia, insulinemia and glycated hemoglobin level, HOMA-IR and HOMA-beta indices, plasma activities of hepatocellular enzymes, lipid peroxidation index, CD3(+)/CD4(+) and CD3(+)/CD4(+) and pro-inflammatory cytokines when decreased antioxidant status in liver was noted. Most of our study indicates that malathion promotes insulin resistance, inflammation and Hepatosteatosis in subchronic model of exposure. On the basis of biochemical and molecular findings, it is concluded that insulin resistance induced by malathion occurs through oxidative stress and related pro-inflammatory markers in a way to result in a reduced function of insulin in liver cells.","","","RefMan","","","","","","","","","" "Unknown","Unknown","Unknown","Unknown","","","2015","Liebman, K. A., Pinto, J., Valle, J., Palomino, M., Vizcaino, L., Brogdon, W., Lenhart, A.","Novel mutations on the ace-1 gene of the malaria vector Anopheles albimanus provide evidence for balancing selection in an area of high insecticide resistance in Peru","Malaria journal","14:74","6131a30c-5522-4984-ad7e-388aa48e711a","","BACKGROUND: Resistance to multiple classes of insecticides has been detected in the malaria vector Anopheles albimanus in northwest Peru. Acetylcholinesterase (AChE) insensitivity has previously been associated with resistance to organophosphate (OP) and carbamate (CA) insecticides in arthropods. A single point mutation on the ace-1 gene (G119S) associated with resistance to OPs and CAs has been described previously in four anopheline species, but not in field-collected An. albimanus. The present study aimed to characterize the role of ace-1 in conferring resistance to both OPs and CAs in the An. albimanus population in Tumbes, Peru. METHODS: The frequency and intensity of resistance to OPs and CAs was quantified through bioassays of female An. albimanus collected between 2012 and 2014, and the presence of insensitive AChE was confirmed using biochemical assays. A portion of the ace-1 gene flanking codon 119 was amplified and sequenced from individuals used in the bioassays and biochemical assays, as well as from historical samples collected in 2008. Statistical analyses were conducted to determine: (1) associations between genotype and AChE insensitivity; and, (2) associations between genotype and resistance phenotype. RESULTS: After confirming high levels of resistance to fenitrothion, malathion, and bendiocarb through bioassays, two novel polymorphisms were identified at the first and second loci of codon 119, with all individuals from the 2012-2014 collections being heterozygous at the first base (G/T) and either heterozygous (G/C) or homozygous mutants (C/C) at the second base. Based on sequence data from historical samples, these mutations arose prior to 2008, but became fixed in the population between 2008 and 2012. Homozygotes at the second locus had significantly higher levels of AChE insensitivity than heterozygotes ($p < 0.05$). Individuals phenotypically susceptible to

OPs and CAs were more likely to be heterozygous at the second locus (p <0.01). Cloning identified four individuals each containing three distinct genotypes, suggesting that a duplication of the ace-1 gene may have occurred. CONCLUSIONS: The occurrence of heterozygotes at two loci and the presence of three genotypes in four individuals suggest that balancing selection could be maintaining OP and CA resistance in this population, while minimizing associated fitness costs.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","2013","Low, V. L., Chen, C. D., Lim, P. E., Lee, H. L., Lim, Y. A., Tan, T. K., Sofian-Azirun, M.","First molecular genotyping of insensitive acetylcholinesterase associated with malathion resistance in Culex quinquefasciatus Say populations in Malaysia","Pest management science","69(12):1362-8","d6191cf1-669d-4e6f-8e89-04b221a17a06","","BACKGROUND: Given that there is limited available information on the insensitive acetylcholinesterase in insect species in Malaysia, the present study aims to detect the presence of G119S mutation in the acetylcholinesterase gene of Culex quinquefasciatus from 14 residential areas across 13 states and a federal territory in Malaysia. RESULTS: The ace-1 sequence and PCR-RFLP test revealed the presence of glycine-serine ace-1 mutation in the wild populations of Cx. quinquefasciatus. Both direct sequencing and PCR-RFLP methods demonstrated similar results and revealed the presence of a heterozygous genotype at a very low frequency (18 out of 140 individuals), while a homozygous resistant genotype was not detected across any study site in Malaysia. In addition, statistical analysis also revealed that malathion resistance is associated with the frequency of ace-1(R) in Cx. quinquefasciatus populations. CONCLUSION: This study has demonstrated the first field-evolved instance of G119S mutation in Malaysian populations. Molecular identification of insensitive acetylcholinesterase provides significant insights into the evolution and adaptation of the Malaysian Cx. quinquefasciatus populations.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","2012","Lu, X. T., Ma, Y., Wang, C., Zhang, X. F., da Jin, Q., Huang, C. J.","Cytotoxicity and DNA damage of five organophosphorus pesticides mediated by oxidative stress in PC12 cells and protection by vitamin E","","47(5):445-454","a95dfa40-abe4-473c-9d8d-ddd98f2ec072","","Previous studies have demonstrated that pesticides could induce cytotoxicity and genotoxicity in vivo and in vitro, and that oxidative stress may be an important factor involved. However, investigations comparing the capability of different organophosphorous (OP) compounds to induce cytotoxicity, genotoxicity and oxidative stress are limited. Hence, the aim of this paper was to access the cytotoxic and genotoxic effects of five OPs or metabolites, Acephate (ACE), Methamidophos (MET), Chloramidophos (CHL), Malathion (MAT) and Malaoxon (MAO), and to clarify the role of oxidative stress, using PC12 cells. The results demonstrated that MET, MAT and MAO caused significant inhibition of cell viability and increased DNA damage in PC12 cells at 40 mg L-1. MAO was more toxic than the other OPs. ACE, MET, MAT and MAO increased the levels of intracellular reactive oxygen species (ROS) and malondialdehyde (MDA), and decreased the activity of superoxide dismutase (SOD), catalase (CAT) and glutathione (GSH) at 20 mg L-1 and 40 mg L-1 to different degrees. Pre-treatment with vitamin E(600 Î¼M)caused a significant attenuation in the cytotoxic and genotoxic effect; pre-treatment reversed subsequent OP-induced elevation of peroxidation products and the decline of anti-oxidant enzyme activities. These results indicate that oxidative damage is likely to be an initiating event that contributes to the OP-induced cytotoxicity. Â© 2012 Copyright Taylor and

Francis Group, LLC.","","","RefMan","","","","","","","","","" "Unknown","Unknown","Unknown","Unknown","","","2013","Ma, R., Kaundun, S. S., Tranel, P. J., Riggins, C. W., McGinness, D. L., Hager, A. G., Hawkes, T., McIndoe, E., Riechers, D. E.","Distinct detoxification mechanisms confer resistance to mesotrione and atrazine in a population of waterhemp","Plant physiology","163(1):363-77","b23be430-dfd8-417d-ac79-5620b93058b2","","Previous research reported the first case of resistance to mesotrione and other 4-hydroxyphenylpyruvate dioxygenase (HPPD) herbicides in a waterhemp (Amaranthus tuberculatus) population designated MCR (for McLean County mesotrione- and atrazine-resistant). Herein, experiments were conducted to determine if target site or nontarget site mechanisms confer mesotrione resistance in MCR. Additionally, the basis for atrazine resistance was investigated in MCR and an atrazine-resistant but mesotrione-sensitive population (ACR for Adams County mesotrione-sensitive but atrazine-resistant). A standard sensitive population (WCS for Wayne County herbicide-sensitive) was also used for comparison. Mesotrione resistance was not due to an alteration in HPPD sequence, HPPD expression, or reduced herbicide absorption. Metabolism studies using whole plants and excised leaves revealed that the time for 50% of absorbed mesotrione to degrade in MCR was significantly shorter than in ACR and WCS, which correlated with previous phenotypic responses to mesotrione and the quantity of the metabolite 4-hydroxy-mesotrione in excised leaves. The cytochrome P450 monooxygenase inhibitors malathion and tetcyclacis significantly reduced mesotrione metabolism in MCR and corn (Zea mays) excised leaves but not in ACR. Furthermore, malathion increased mesotrione activity in MCR seedlings in greenhouse studies. These results indicate that enhanced oxidative metabolism contributes significantly to mesotrione resistance in MCR. Sequence analysis of atrazine-resistant (MCR and ACR) and atrazine-sensitive (WCS) waterhemp populations detected no differences in the psbA gene. The times for 50% of absorbed atrazine to degrade in corn, MCR, and ACR leaves were shorter than in WCS, and a polar metabolite of atrazine was detected in corn, MCR, and ACR that cochromatographed with a synthetic atrazine-glutathione conjugate. Thus, elevated rates of metabolism via distinct detoxification mechanisms contribute to mesotrione and atrazine resistance within the MCR population.","","","RefMan","","","","","","","","","" "Unknown","Unknown","Unknown","Unknown","","","2014","Maestre-Serrano, R., Gomez-Camargo, D., Ponce-Garcia, G., Flores, A. E.","Susceptibility to insecticides and resistance mechanisms in Aedes aegypti from the Colombian Caribbean Region","Pesticide biochemistry and physiology","116:63-73","924d5fc5-7207-486f-b7ed-ec2470b135de","","We determined the susceptibility to insecticides and the biochemical and molecular mechanisms involved in resistance in nine populations of Aedes aegypti (L.) of the Colombian Caribbean region. Bioassays were performed on larvae for susceptibility to temephos and on adults to the insecticides malathion, fenitrothion, pirimiphos-methyl, permethrin, deltamethrin, lambda-cyhalothrin and cyfluthrin. The resistance ratio (RR) for each insecticide in the populations was determined, using the susceptible Rockefeller strain as a susceptible control. Additionally, we evaluated the response of the populations to the diagnostic dose (DD) of the organochlorine pesticide DDT. The following biochemical mechanisms associated with resistance were studied: alpha-esterases, beta-esterases, mixed-function oxidases (MFO), glutathione s-transferases (GST) and insensitive acetylcholinesterase (iAChE) as well as the presence of kdr I1,016 mutation and its frequency. All populations studied showed susceptibility to the organophosphates evaluated (RR < 5-fold), except for the Puerto Colombia and Soledad

populations which showed high resistance (RR 15-fold) and moderate resistance (RR 5-fold) to temephos, respectively, and Sincelejo (Sucre) with moderate resistance to pirimiphos-methyl (RR 5-fold). All populations evaluated with DD of DDT were found to be resistant with 2-28% of mortality. Variability was observed in the resistance to pyrethroids: permethrin (RR 1.2- to 30.8-fold), deltamethrin RR 0.9- to 37.8-fold), lambda-cyalothrin (RR 3.4- to 83-fold) and cyfluthrin (RR 0.3- to 33.8-fold). Incipiently alpha-esterases and MFO levels were found in the Valledupar population; MFO showed the same profile in Cienaga and GST in the Sincelejo population, all other populations showed unaltered profiles of the enzymes evaluated. The kdr I1,016 mutation was found in all populations evaluated with variability in its allelic and genotypic frequencies.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","2008","Magana, C., Hernandez-Crespo, P., Brun-Barale, A., Couso-Ferrer, F., Bride, J. M., Castanera, P., Feyereisen, R., Ortego, F.","Mechanisms of resistance to malathion in the medfly Ceratitis capitata","Insect biochemistry and molecular biology","38(8):756-62","39c18894-0fb9-4cee-8b06-e6fc93b42014","","Target site insensitivity and metabolic resistance mediated by esterases have been previously suggested to be involved in resistance to malathion in a field-derived strain (W) of Ceratitis capitata. In the present study, we have obtained the coding sequence for acetylcholinesterase (AChE) gene (Ccace) of C. capitata. An allele of Ccace carrying only a point mutation Gly328Ala (Torpedo numbering) adjacent to the glutamate of the catalytic triad was found in individuals of the W strain. Adult flies homozygotes for this mutant allele showed reduced AChE activity and less sensitivity to inhibition by malaoxon, showing that target site insensitivity is one of the factors of malathion resistance. In addition, all individuals from the resistant W strain showed reduced aliesterase activity, which has been associated with specific malathion resistance in higher Diptera. However, the alphaE7 gene (CcalphaE7), sequenced in susceptible and resistant individuals, did not carry any of the mutations associated with organophosphorus insecticide resistance in other Diptera. Another esterase mechanism, perhaps a carboxylesterase selective for malathion, in addition to mutant AChE, thus contributes to malathion resistance in C. capitata.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","2015","Mandrich, L., Cerreta, M., Manco, G.","An Engineered Version of Human PON2 Opens the Way to Understand the Role of Its Post-Translational Modifications in Modulating Catalytic Activity","PloS one","10(12):e0144579","7dfa905c-4050-4d9b-b26e-bdaafc9a15e0","","The human paraoxonase 2 (PON2) has been described as a highly specific lactonase hydrolysing the quorum sensing molecule N-(3-oxododecanoyl)-L-homoserine lactone (3OC12-HSL) and having secondary esterase but not phosphotriesterase activity, in contrast with the related enzymes PON1 and PON3. It has been suggested that PON2 enzyme activity is dependent on glycosylation and its N-terminal region has been recently demonstrated to be a transmembrane domain mediating association to membranes. In the present study we describe a mutated form of PON2, lacking the above N-terminal region, which has been further stabilized by the insertion of six amino acidic substitutions. The engineered version, hence forth called rPON2, has been over-expressed in E.coli, refolded from inclusion bodies and purified, yielding an enzyme with the same characteristics as the full length enzyme. Therefore the first conclusion of this work was that the catalytic activity is independent from the N-terminus and protein glycosylation. The kinetic characterization confirmed the primary activity on 3OC12-HSL; accordingly, in vitro

experiments of inhibition of the biofilm formed by Pseudomonas aeruginosa (PAO1) have demonstrated that rPON2 is more effective than PON1. In addition, we observed small but significant activity against organophosphorothiotes pesticides, m-parathion, coumaphos and malathion.The availability of fair amount of active protein allowed to pinpoint, by mass-spectrometry, ubiquitination of Lys 168 induced in rPON2 by HeLa extract and to correlate such post-translational modification to the modulation of catalytic activity. A mutational analysis of the modified residue confirmed the result.","","","RefMan","","","","","","","","","","Unknown","Unknown","Unknown","Unknown","","","2014","Marcombe, S., Farajollahi, A., Healy, S. P., Clark, G. G., Fonseca, D. M.","Insecticide resistance status of United States populations of Aedes albopictus and mechanisms involved","","9(7)","ad20ed02-750d-42e2-bad8-40525d6e8cb7","","Aedes albopictus (Skuse) is an invasive mosquito that has become an important vector of chikungunya and dengue viruses. Immature Ae. albopictus thrive in backyard household containers that require treatment with larvicides and when adult populations reach pest levels or disease transmission is ongoing, adulticiding is often required. To assess the feasibility of control of USA populations, we tested the susceptibility of Ae. albopictus to chemicals representing the main insecticide classes with different modes of action: organochlorines, organophosphates, carbamates, pyrethroids, insect growth regulators (IGR), naturalytes, and biolarvicides. We characterized a susceptible reference strain of Ae. albopictus, ATM95, and tested the susceptibility of eight USA populations to five adulticides and six larvicides. We found that USA populations are broadly susceptible to currently available larvicides and adulticides. Unexpectedly, however, we found significant resistance to dichlorodiphenyltrichloroethane (DDT) in two Florida populations and in a New Jersey population. We also found resistance to malathion, an organophosphate, in Florida and New Jersey and reduced susceptibility to the IGRs pyriproxyfen and methoprene. All populations tested were fully susceptible to pyrethroids. Biochemical assays revealed a significant upregulation of GSTs in DDT-resistant populations in both larval and adult stages. Also, Î²-esterases were up-regulated in the populations with suspected resistance to malathion. Of note, we identified a previously unknown amino acid polymorphism (Phe â†' Leu) in domain III of the VGSC, in a location known to be associated with pyrethroid resistance in another container-inhabiting mosquito, Aedes aegypti L. The observed DDT resistance in populations from Florida may indicate multiple introductions of this species into the USA, possibly from tropical populations. In addition, the mechanisms underlying DDT resistance often result in pyrethroid resistance, which would undermine a remaining tool for the control of Ae. albopictus. Continued monitoring of the insecticide resistance status of this species is imperative. Â© 2014 Marcombe et al.","","","RefMan","","","","","","","","","","Unknown","Unknown","Unknown","Unknown","","","2003","Masoud, L., Vijayasarathy, C., Fernandez-Cabezudo, M., Petroianu, G., Saleh, A. M.","Effect of malathion on apoptosis of murine L929 fibroblasts: a possible mechanism for toxicity in low dose exposure","Toxicology","185(1-2):89-102","41a2cc89-77b1-41a4-b702-13121bc17458","","While acute organophosphorous compound poisoning due to inhibition of acetylcholinesterase is a well-established clinical entity, the existence of chronic poisoning due to exposure to low levels of organophosphorous compounds (below the threshold required for cholinergic clinical symptoms) is a hotly debated issue. In this study, we have evaluated the effects of noncholinergic doses of malathion (0.01-20 microM) on apoptosis of murine L929 fibroblasts. Employing flow cytometric and caspase

activation analyses we demonstrate that malathion induces apoptosis in L929 cells in a dose- and time-dependent manner. The initiator caspases (caspase-8 and caspase-9) as well as the effector caspase (caspase-3) were activated by the treatment of L929 cells with malathion. Exposure of L929 cells to malathion in the presence of a general inhibitor of caspase, z-VAD-FMK abolished the apoptotic effect of the compound. In addition, malathion induced an increase in the expression of the pro-apoptotic protein p53. However, the induction of p53 expression was subsequent to activation of the caspase cascades. The present findings suggest, that the cytotoxicity of malathion at noncholinergic doses is mediated through caspase-dependent apoptosis.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","2007","Matambo, T. S., Abdalla, H., Brooke, B. D., Koekemoer, L. L., Mnzava, A., Hunt, R. H., Coetzee, M.","Insecticide resistance in the malarial mosquito Anopheles arabiensis and association with the kdr mutation","Medical and veterinary entomology","21(1):97-102","18dfcd78-527c-407b-907e-36aa366ecd76","","A colony of Anopheles arabiensis Patton (Diptera: Culicidae) from the Sennar region of Sudan was selected for resistance to dichlorodiphenyltrichloroethane (DDT). Adults from the F-16 generation of the resistant strain were exposed to all four classes of insecticides approved for use in malaria vector control and showed high levels of resistance to them all (24-h mortalities: malathion, 16.7%; bendiocarb, 33.3%; DDT, 12.1%; dieldrin, 0%; deltamethrin, 24.0%; permethrin, 0%). Comparisons between the unselected base colony and the DDT-resistant strain showed elevated glutathione-S-transferase (P<0.05) in both sexes and elevated esterases (P<0.05) in males only. The Leu-Phe mutation in the sodium channel gene was detected by polymerase chain reaction and sequencing, but showed no correlation with the resistant phenotype. These results do not provide any explanation as to why this colony exhibits such widespread resistance and further studies are needed to determine the precise mechanisms involved. The implications for malaria vector control in central Sudan are serious and resistance management (e.g. through the rotational use of different classes of insecticides) is recommended.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","2015","Misra, B. R., Gore, M.","Malathion Resistance Status and Mutations in Acetylcholinesterase Gene (Ace) in Japanese Encephalitis and Filariasis Vectors from Endemic Area in India","Journal of medical entomology","52(3):442-6","302a5891-a255-4c9a-a95c-193ccdb69e66","","Japanese encephalitis (JE) and lymphatic filariasis (LF) are endemic in estern part of Uttar Pradesh in India and transmitted by Culex mosquitoes (Diptera: Culicidae). JE vaccination and mass drug administration for JE and LF management is being undertaken respectively. In addition to this, indoor residual spraying and fogging are used for the control of mosquito vectors. Organophosphate resistance in mosquito is dependent on alteration in acetylcholinesterase (Ace) gene. Hence, it is important to evaluate organophosphate resistance in Culex tritaeniorhynchus Giles (JE vector) and Culex quinquefasciatus Say (LF vector). The current study showed the presence of resistant populations and F331W mutation in Cx. tritaeniorhynchus and G119S mutation in Cx. quinquefasciatus insensitive Ace genes. Resistant populations of these two vectors increase the chances of spreading of resistance in the natural population and may cause failure of intervention programs that include organophosphates against these two vectors in future.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","2012","Misra, J. R., Horner, M. A., Lam, G., Thummel, C. S.","Transcriptional regulation of xenobiotic detoxification in

drosophila","","26","7cce5b28-90d6-4e9b-8834-b9f2359d67d5","","Xenobiotic compounds pose a constant threat to the survival of all organisms and to overcome this, animals mount an elaborate transcriptional response, regulating a battery of enzymes that detoxify these compounds. Several transcription factors have been identified in vertebrates that regulate this response. In contrast, little is known about this pathway in insects. We show that the Drosophila Nrf2 ortholog, CncC, is a central regulator of xenobiotic detoxification responses. A binding site for CncC and its heterodimer partner Maf is sufficient and necessary for robust transcriptional responses to three xenobiotic compounds, phenobarbital (PB), chlorpromazine, and caffeine. Genetic manipulations that alter the levels of CncC, or its negative regulator Keap1, lead to predictable changes in xenobiotic-inducible gene expression. Transcriptional profiling studies reveal that more than half of the genes regulated by PB are also controlled by CncC. Consistent with these effects on detoxification gene expression, activation of the CncC/Keap1 pathway in Drosophila is sufficient to confer resistance to the pesticide malathion. Further, in the two pesticide-resistant strains of Drosophila, the pathway is constitutively active, leading to overexpression of several detoxification genes. Our current efforts are aimed at identifying the mutations that constitutively activate the pathway in these strains.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","2008","Miyo, T., Oguma, Y.","Genetic variation in susceptibility to organophosphate insecticides within the Katsunuma population of drosophila melanogaster","","83(6):519","465a40ed-36b5-4c5b-a9de-b70da0bc78b2","","We have mapped two resistance factors conferring resistance to organophosphates within the Katsunuma population of D. melanogaster (72nd Annual Meeting). With regard to the second chromosome factor, we tested susceptibility to malathion of more than 50 recombinant inbred lines between ltd and vg. ANOVA showed highly significant variation in susceptibility to malathion between lines. In addition, susceptibility of the second chromosome resistant line to malathion was increased with additional application of the cytochrome P450 inhibitor, suggesting that it could be a member of the Cyp gene family located between ltd and vg. With regard to the third chromosome factor, acetylcholinesterase of resistant lines was about 15 times more insensitive to fenitroxon and about twice to carbaryl than that of susceptible lines, suggesting it was a mutated acetylcholinesterase. Furthermore, genetic variation at three sites in the acetylcholinesterase gene was examined for Katsunuma population samples collected in 2006, using the allele-specific PCR. It was revealed that there were high frequencies of resistant-type mutations at the three sites in the Katsunuma population.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","2011","Moore, P. D., Patlolla, A. K., Tchounwou, P. B.","Cytogenetic evaluation of malathion-induced toxicity in Sprague-Dawley rats","Mutation research","725(1-2):78-82","8e6dbd8c-e4f9-4175-bdde-33cdf8017a85","","Malathion is a well known pesticide and is commonly used in many agricultural and non-agricultural settings. Its toxicity has been attributed primarily to the accumulation of acetylcholine (Ach) at nerve junctions, due to the inhibition of acetylcholinesterase (AChE), and consequently overstimulation of the nicotinic and muscarinic receptors. However, the genotoxicity of malathion has not been adequately studied; published studies suggest a weak interaction with the genetic material. In the present study, we investigated the genotoxic potential of malathion in bone marrow cells and peripheral blood obtained from Sprague-Dawley rats using chromosomal

aberrations (CAs), mitotic index (MI), and DNA damage as toxicological endpoints. Four groups of four male rats, each weighing approximately 60 +/- 2g, were injected intraperitoneally (i.p.) once a day for five days with doses of 2.5, 5, 10, and 20mg/kg body weight (BW) of malathion dissolved in 1% DMSO. The control group was made up of four animals injected with 1% DMSO. All the animals were sacrificed 24h after the fifth day treatment. Chromosome preparations were obtained from bone marrow cells following standard protocols. DNA damage in peripheral blood leukocytes was determined using alkaline single-cell gel electrophoresis (comet assay). Malathion exposure significantly increased the number of structural chromosomal aberrations (CAs) and the percentages of DNA damage, and decreased the mitotic index (MI) in treated groups when compared with the control group. Our results demonstrate that malathion has a clastogenic/genotoxic potential as measured by the bone marrow CA and comet assay in Sprague-Dawley rats.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","2010","Moore, P. D., Yedjou, C. G., Tchounwou, P. B.","Malathion-induced oxidative stress, cytotoxicity, and genotoxicity in human liver carcinoma (HepG2) cells","Environmental toxicology","25(3):221-6","d83a9fef-7bc5-461e-9b13-f8c9e423d8f4","","Malathion is an organophosphate pesticide that is known for its high toxicity to insects and low to moderate potency to humans and other mammals. Its toxicity has been associated with the inhibition of acetylcholinesterase activity, leading to the interference with the transmission of nerve impulse, accumulation of acetylcholine at synaptic junctions, and subsequent induction of adverse health effects including headache, dizziness, nausea, vomiting, bradycardia, and miosis. Oxidative stress (OS) has been reported as a possible mechanism of malathion toxicity in humans. Hence, the aim of this study was to examine the role of OS in malathion-induced cytotoxicity and genotoxicity. To achieve this goal, MTT, lipid peroxidation, and single cell gel electrophoresis (Comet) assays were performed, respectively, to evaluate the levels of cell viability, malondialdehyde (MDA) production, and DNA damage in human liver carcinoma (HepG(2)) cells. Study results indicated that malathion is mitogenic at lower levels of exposure, and cytotoxic at higher levels of exposure. Upon 48 h of exposure, the average percentages of cell viability were 100% +/- 11%, 117% +/- 15%, 86% +/- 15%, 35% +/- 9%, and 27% +/- 7% for 0, 6, 12, 18, and 24 mM, respectively. In the lipid peroxidation assay, the concentrations of MDA produced were 12.55 +/- 0.16, 20.65 +/- 0.27, 31.1 +/- 0.40, 34.75 +/- 0.45, and 15.1 +/- 0.20 muM in 0, 6, 12, 18, and 24 mM malathion, respectively. The Comet assay showed a significant increase in DNA damage at the 24 mM malathion exposure. Taken together, our results indicate that malathion exposure at higher concentrations induces cytotoxic and genotoxic effects in HepG(2) cells, and its toxicity may be mediated through OS as evidenced by a significant production of MDA, an end product of lipid peroxidation.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","2010","Morgan, J. C., Irving, H., Okedi, L. M., Steven, A., Wondji, C. S.","Pyrethroid resistance in an Anopheles funestus population from Uganda","PloS one","5(7):e11872","12b0f5a3-1069-47d8-ac32-126b77df1575","","BACKGROUND: The susceptibility status of Anopheles funestus to insecticides remains largely unknown in most parts of Africa because of the difficulty in rearing field-caught mosquitoes of this malaria vector. Here we report the susceptibility status of the An. funestus population from Tororo district in Uganda and a preliminary characterisation of the putative resistance mechanisms involved. METHODOLOGY/PRINCIPAL FINDINGS: A new forced egg laying technique used in this study

significantly increased the numbers of field-caught females laying eggs and generated more than 4000 F1 adults. WHO bioassays indicated that An. funestus in Tororo is resistant to pyrethroids (62% mortality after 1 h exposure to 0.75% permethrin and 28% mortality to 0.05% deltamethrin). Suspected DDT resistance was also observed with 82% mortality. However this population is fully susceptible to bendiocarb (carbamate), malathion (organophosphate) and dieldrin with 100% mortality observed after exposure to each of these insecticides. Sequencing of a fragment of the sodium channel gene containing the 1014 codon conferring pyrethroid/DDT resistance in An. gambiae did not detect the L1014F kdr mutation but a correlation between haplotypes and resistance phenotype was observed indicating that mutations in other exons may be conferring the knockdown resistance in this species. Biochemical assays suggest that resistance in this population is mediated by metabolic resistance with elevated level of GSTs, P450s and pNPA compared to a susceptible strain of Anopheles gambiae. RT-PCR further confirmed the involvement of P450s with a 12-fold over-expression of CYP6P9b in the Tororo population compared to the fully susceptible laboratory colony FANG. CONCLUSION: This study represents the first report of pyrethroid/DDT resistance in An. funestus from East Africa. With resistance already reported in southern and West Africa, this indicates that resistance in An. funestus may be more widespread than previously assumed and therefore this should be taken into account for the implementation and management of vector control programs in Africa.","","","RefMan","","","","","","","","","","Unknown","Unknown","Unknown","Unknown","","","2012","Mostafalou, S., Eghbal, M. A., Nili-Ahmadabadi, A., Baeeri, M., Abdollahi, M.","Biochemical evidence on the potential role of organophosphates in hepatic glucose metabolism toward insulin resistance through inflammatory signaling and free radical pathways","Toxicology and industrial health","28(9):840-51","efc691cf-258c-44d4-86d8-41d326b0ba46","","Several studies show that organophosphate pesticides exert several effects on glucose homeostasis. The current study investigates the influence of subchronic exposure to malathion (MT) on hepatic gluconeogenesis in relation to acetyl cholinesterase (AChE) inhibition, oxidative stress and inflammatory response in the rat. MT was administered by gavage at doses of 25, 50 and 100 mg/kg for 32 days. Fasting hyperglycemia was seen in line with an increased activity of hepatic phosphoenolpyruvate carboxykinase, glucose 6-phosphatase and tumor necrosis factor alpha. In addition to the impaired glucose tolerance and inhibition of AChE in a dose-dependent manner, there were significant increases in hepatic lipid peroxidation, carbonyl groups and 8-deoxyguanosine as the biomarkers of reactive oxygen species-mediated damage to lipid, protein and DNA, respectively. Altered quality of the liver in glucose production especially gluconeogenesis could be a compensatory mechanism against MT toxicity or even result in tissue damage. MT-induced insulin resistance in the liver occurs through oxidative and inflammatory signaling pathways.","","","RefMan","","","","","","","","","","Unknown","Unknown","Unknown","Unknown","","","2013","Mostafalou, S., Karami-Mohajeri, S., Abdollahi, M.","Environmental and population studies concerning exposure to pesticides in Iran: A comprehensive review","","15(12)","eb336cd0-ac89-41b7-b4be-9d1aa4f2bf49","","Pesticides are widely used in Iranian agriculture and this has made a major toxicological concern among health professionals. The objective of this study is to explore national data about pesticides toxicity. All relevant databases such as Google Scholar, PubMed, and Scopus in a time period of 1960 to 2012 were searched for the keywords ""Pesticides, Iran, Environment, and Population studies"". A total of 57

studies were found relevant and then included into study. Almost all non-experimental studies carried out in Iran were classified into two main categories of residue assessment in different samples and toxic effects on human. Depending on the dose and duration of exposure, toxic effects of pesticides have been studied in two classifications including acute toxicity or acute poisoning and chronic toxicity. High extent of pesticides have been used during the past decade in Iran while no enough proper studies were done to explore their possible toxic effects in the environment and the people.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","2001","Mourya, D. T., Gokhale, M. D., Barde, P. V., Deobagkar, D. N.","Highly-substrate active isoenzyme acetylcholinesterase-II, in rosy eye mutant of Aedes aegypti mosquito","Indian journal of experimental biology","39(8):807-10","8c3f4f15-4723-4bc6-abf1-be5ac459dd6a","","Insecticide bioassays were carried out on larvae and adults of rosy eye mutant and wildtype strains of A. aegypti. Both the strains were equally susceptible to DDT, malathion and deltamethrin. Biochemical assays showed an increase in acetylcholinesterase enzyme (AChE) activity in all the stages of mutant strain with both the substrates i.e. acetylthiocholine iodide and S-butyrylthiocholine iodide. However, there was no difference in the percent inhibition of enzyme activity with propoxur in these two strains. Polyacrylamide gel electrophoresis performed in native conditions on the homogenates of adults of rosy eye mosquitoes showed that AChE-II allele was highly active with the substrate acetylthiocholine iodide as compared to wildtype strain. Frequency of the highly active AChE-II allele in the mutant strain was about 68%, whereas it was about 5% in the wildtype strain.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","2014","Mulamba, C., Riveron, J. M., Ibrahim, S. S., Irving, H., Barnes, K. G., Mukwaya, L. G., Birungi, J., Wondji, C. S.","Widespread pyrethroid and DDT resistance in the major malaria vector anopheles funestus in East Africa is driven by metabolic resistance mechanisms","","9(10)","d1733c7e-1ce8-4e87-a5e9-65d59edc380a","","Background: Establishing the extent, geographical distribution and mechanisms of insecticide resistance in malaria vectors is a prerequisite for resistance management. Here, we report a widespread distribution of insecticide resistance in the major malaria vector An. funestus across Uganda and western Kenya under the control of metabolic resistance mechanisms. Copyright: Methodology/Principal Findings: Female An. funestus collected throughout Uganda and western Kenya exhibited a Plasmodium infection rate between 4.2 to 10.4%. Widespread resistance against both type I (permethrin) and II (deltamethrin) pyrethroids and DDT was observed across Uganda and western Kenya. All populations remain highly susceptible to carbamate, organophosphate and dieldrin insecticides. Knockdown resistance plays no role in the pyrethroid and DDT resistance as no kdr mutation associated with resistance was detected despite the presence of a F1021C replacement. Additionally, no signature of selection was observed on the sodium channel gene. Synergist assays and qRTPCR indicated that metabolic resistance plays a major role notably through elevated expression of cytochrome P450s. DDT resistance mechanisms differ from West Africa as the L119F-GSTe2 mutation only explains a small proportion of the genetic variance to DDT resistance. Conclusion: The extensive distribution of pyrethroid and DDT resistance in East African An. funestus populations represents a challenge to the control of this vector. However, the observed carbamate and organophosphate susceptibility offers alternative solutions for resistance

management.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","2008","Munhenga, G., Masendu, H. T., Brooke, B. D., Hunt, R. H., Koekemoer, L. K.","Pyrethroid resistance in the major malaria vector Anopheles arabiensis from Gwave, a malaria-endemic area in Zimbabwe","Malaria journal","7:247","76daf511-aada-48ea-b146-50d2021ea1c4","","BACKGROUND: Insecticide resistance can present a major obstacle to malaria control programmes. Following the recent detection of DDT resistance in Anopheles arabiensis in Gokwe, Zimbabwe, the underlying resistance mechanisms in this population were studied. METHODS: Standard WHO bioassays, using 0.75% permethrin, 4% DDT, 5% malathion, 0.1% bendiocarb and 4% dieldrin were performed on wild-collected adult anopheline mosquitoes and F1 progeny of An. arabiensis reared from wild-caught females. Molecular techniques were used for species identification as well as to identify knockdown resistance (kdr) and ace-1 mutations in individual mosquitoes. Biochemical assays were used to determine the relative levels of detoxifying enzyme systems including non-specific esterases, monooxygenases and glutathione-S-transferases as well as to detect the presence of an altered acetylcholine esterase (AChE). RESULTS: Anopheles arabiensis was the predominant member of the Anopheles gambiae complex. Of the 436 An. arabiensis females, 0.5% were positive for Plasmodium falciparum infection. WHO diagnostic tests on wild populations showed resistance to the pyrethroid insecticide permethrin at a mean mortality of 47% during February 2006 and a mean mortality of 68.2% in January 2008. DDT resistance (68.4% mean mortality) was present in February 2006; however, two years later the mean mortality was 96%. Insecticide susceptibility tests on F1 An. arabiensis families reared from material from two separate collections showed an average mean mortality of 87% (n = 758) after exposure to 4% DDT and 65% (n = 587) after exposure to 0.75% permethrin. Eight families were resistant to both DDT and permethrin. Biochemical analysis of F1 families reared from collections done in 2006 revealed high activity levels of monooxygenase (48.5% of families tested, n = 33, p < 0.05), glutathione S-transferase (25.8% of families tested, n = 31, p < 0.05) and general esterase activity compared to a reference susceptible An. arabiensis colony. Knockdown resistance (kdr) and ace-IR mutations were not detected. CONCLUSION: This study confirmed the presence of permethrin resistance in An. arabiensis populations from Gwave and emphasizes the importance of periodic and ongoing insecticide susceptibility testing of malaria vector populations whose responses to insecticide exposure may undergo rapid change over time.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","2010","MuÃ±oz, B., Albores, A.","The role of molecular biology in the bio monitoring of human exposure to chemicals","","11(11):4511-4525","b59e0521-d305-431b-bae3-f50d6214989c","","Exposure to different substances in an occupational environment is of utmost concern to global agencies such as the World Health Organization and the International Labour Organization. Interest in improving work health conditions, particularly of those employees exposed to noxious chemicals, has increased considerably and has stimulated the search for new, more specific and selective tests. Recently, the field of molecular biology has been indicated as an alternative technique for monitoring personnel while evaluating work-related pathologies. Originally, occupational exposure to environmental toxicants was assessed using biochemical techniques to determine the presence of higher concentrations of toxic compounds in blood, urine, or other fluids or tissues; results were used to evaluate potential health risk. However, this approach only estimates the

presence of a noxious chemical and its effects, but does not prevent or diminish the risk. Molecular biology methods have become very useful in occupational medicine to provide more accurate and opportune diagnostics. In this review, we discuss the role of the following common techniques: (1) Use of cell cultures; (2) evaluation of gene expression; (3) the ""omic"" sciences (genomics, transcriptomics, proteomics and metabolomics) and (4) bioinformatics. We suggest that molecular biology has many applications in occupational health where the data can be applied to general environmental conditions. Â© 2010 by the authors.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","2011","Muturi, E. J., Kim, C. H., Alto, B. W., Berenbaum, M. R., Schuler, M. A.","Larval environmental stress alters Aedes aegypti competence for Sindbis virus","Tropical medicine & international health : TM & IH","16(8):955-64","bb27be98-6306-49be-a010-84df55e71bf5","","OBJECTIVE: To evaluate how stress at the larval stage alters adult mosquito performance and susceptibility to viral infection. METHODS: We used a model system consisting of Sindbis virus (SINV) and the yellow fever mosquito Aedes aegypti. Larvae were either reared under optimal conditions (control) or exposed to one of four types of stressors; suboptimal nutrients, starvation, elevated temperature, and a low dose of the insecticide malathion and adult females were fed SINV infectious blood meal. Differential expressions of stress, immune-specific and detoxification genes was measured in fourth instar larvae (HSP70, HSP83, cecropin, defensin, transferrin and CYP6Z6) and 3-day-old females (cecropin, defensin, transferrin) to identify plausible molecular mechanisms associated with mosquito response to stress. RESULTS: There were stress-specific variations in mosquito performance (survival, development time, female size), but all stressors had a consistent effect of significantly increasing susceptibility to viral infection and dissemination relative to the controls. Three genes were up-regulated in fourth instar larvae exposed to temperature stress (cecropin, defensin and CYP6Z6) compared to single genes in suboptimal nutrient (cecropin) and malathion (transferrin) stress treatments and down-regulation of all the six genes in starvation treatments. In adult samples, transferrin was up-regulated in all but starvation treatments while defensin was up-regulated in starvation and temperature stress treatments. CONCLUSIONS: Stress during larval development may cause alterations in adult mosquito phenotype and immunity that can increase their susceptibility to pathogens.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","2014","Naqvi, T., Warden, A. C., French, N., Sugrue, E., Carr, P. D., Jackson, C. J., Scott, C.","A 5000-fold increase in the specificity of a bacterial phosphotriesterase for malathion through combinatorial active site mutagenesis","PloS one","9(4):e94177","03de80f6-9fa5-4515-8c9e-18a6a720aa62","","Phosphotriesterases (PTEs) have been isolated from a range of bacterial species, including Agrobcaterium radiobacter (PTEAr), and are efficient enzymes with broad substrate ranges. The turnover rate of PTEAr for the common organophosphorous insecticide malathion is lower than expected based on its physical properties; principally the pka of its leaving group. In this study, we rationalise the turnover rate of PTEAr for malathion using computational docking of the substrate into a high resolution crystal structure of the enzyme, suggesting that malathion is too large for the PTEAr binding pocket. Protein engineering through combinatorial active site saturation testing (CASTing) was then used to increase the rate of malathion turnover. Variants from a CASTing library in which Ser308 and Tyr309 were mutated

yielded variants with increased activity towards malathion. The most active PTEAr variant carried Ser308Leu and Tyr309Ala substitutions, which resulted in a ca. 5000-fold increase in kcat/KM for malathion. X-ray crystal structures for the PTEAr Ser308Leu\Tyr309Ala variant demonstrate that the access to the binding pocket was enhanced by the replacement of the bulky Tyr309 residue with the smaller alanine residue.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","2013","Navarrete-Meneses, M. P., Betancourt, M., Bonilla, E., Altamirano, M., Salas-LabadÃ-a, C., Reyes, A., PÃ©rez-Vera, P.","In vitro permethrin exposure-induced aberrations in MLL gene","","54:S44","9b367077-25eb-4dc8-849a-566ebb3b29ab","","Introduction: Acute Lymphoblastic Leukemia (ALL) is a hematological malignancy characterized by the presence of chromosomal abnormalities. Translocations involving MLL gene have been detected in 80% of patients under one year old; it is proposed that they arise in utero and are associated with exposure to several agents, including pesticides. Epidemiological studies have shown a strong association between ALL development and pesticides exposure. However there is scarce biological evidence showing the potential of pesticides to induce leukemia-related abnormalities. The aim of this study was to detect alterations in MLL gene induced by permethrin and malathion in human lymphocytes in vitro. Method: Lymphocytes from two healthy volunteers were cultured for 72h and exposed to 200mM of permethrin and malathion for the last 24h. Solvents were used as negative controls. MLL gene was analyzed by FISH. Results: The complexity and heterogeneity of damage was increased by pesticides exposure. The number of abnormal cells tended to increase in cultures treated with malathion but was not statistically significant. Permethrin induced MLL damage (numerical+structural); the number of cells with numerical aberrations was higher, and diversity and complexity of structural abnormalities was also increased ($p<0.05$). Discussion: Aneuploidogen potential of permethrin has not been previously reported; here it was found that can induce numerical abnormalities and increase the diversity of structural aberrations, some of which have been observed in cells exposed to known leukemogenic agents (etoposide). Exposure to permethrin induced ALL-related aberrations that could promote the initial events in the development of this disease.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","2009","Ndjemai, H. N., Patchoke, S., Atangana, J., Etang, J., Simard, F., Bilong, C. F., Reimer, L., Cornel, A., Lanzaro, G. C., Fondjo, E.","The distribution of insecticide resistance in Anopheles gambiae s.l. populations from Cameroon: an update","Transactions of the Royal Society of Tropical Medicine and Hygiene","103(11):1127-38","e33a8447-d098-4825-9a7c-14d000f49320","","Insecticides are a key component of vector-based malaria control programmes in Cameroon. As part of ongoing resistance surveillance efforts, Anopheles gambiae s.l. female mosquitoes were exposed to organochlorine (DDT), a carbamate (bendiocarb), an organophosphate (malathion), and three pyrethroids (deltamethrin, lambda-cyhalothrin and permethrin) in WHO bioassay test kits. Results indicated a higher level of resistance (reduced mortality and knockdown effect) to DDT and pyrethroids in populations of A. gambiae s.s. than in A. arabiensis. The West and East African knockdown resistance (kdr) mutations were found in both species but at much higher frequencies in A. gambiae s.s. The West Africa kdr mutant was also more frequent in the A. gambiae S form than in the M form. No resistance to bendiocarb and malathion was found. Carbamate and organophosphorous compounds could thus be used as alternatives in locations in Cameroon where pyrethroid-resistant populations are

found.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","2005","Newcomb, R. D., Gleeson, D. M., Yong, C. G., Russell, R. J., Oakeshott, J. G.","Multiple mutations and gene duplications conferring organophosphorus insecticide resistance have been selected at the Rop-1 locus of the sheep blowfly, Lucilia cuprina","Journal of molecular evolution","60(2):207-20","4ee4c268-8e57-4b6e-8325-400ce4895af6","","Sequences of the esterase gene alpha E7 were compared across 41 isogenic (IV) strains of the sheep blowfly, Lucilia cuprina, and one strain of the sibling species, L. sericata. The 1.2-kb region sequenced includes sites of two insecticide resistance mutations. Gly137Asp confers resistance to organophosphorus insecticides (OPs), particularly preferring diethyl OPs such as diazinon, while Trp251Leu prefers dimethyl OPs, and particularly malathion, with the additional presence of carboxylester moieties. We found that there are just eight haplotypes among the 41 chromosomes studied: two Gly137Asp containing haplotypes, two Trp251Leu containing haplotypes, and four susceptible haplotypes, including the L. sericata sequence. While phylogenetic analysis of these haplotypes suggests that the Asp137 and Leu251 mutations each arose at least twice, evidence for recombination was detected across the region, therefore single origins for these resistance mutations cannot be ruled out. Levels of linkage disequilibrium in the data are high and significant hitchhiking is indicated by Fay and Wu' s H test but not the Tajima test. A test of haplotype diversity indicates a paucity of diversity compared with neutral expectations. Both these results are consistent with a very recent selective sweep at the Lc alphaE7 locus. Interestingly, gene duplications of three different combinations of OP resistant haplotypes were identified in seven of the isogenic (IV) strains. All three types of duplication involve an Asp137 and a Trp251 haplotype. To examine whether more haplotypes existed before the hypothesised selective sweep, fragments of alpha E7 surrounding the resistance mutations were amplified from pinned material dating back to before OPs were used. Four new sequence haplotypes, not sampled in the survey of extant haplotypes, were obtained that are all associated with susceptibility. This is suggestive of a higher historical level of susceptible allelic diversity at this locus.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","2016","Niang, E. H. A., KonatÃ©, L., Diallo, M., Faye, O., Dia, I.","Patterns of insecticide resistance and knock down resistance (kdr) in malaria vectors An. arabiensis, An. coluzzii and An. gambiae from sympatric areas in Senegal","","9(1)","9b9eaf05-fa32-4d79-9839-8dbdf623fade","","Background: Malaria vector control in Africa relies on insecticides targeting adult mosquito vectors via insecticide treated nets or indoor residual spraying. Despite the proven efficacy of these strategies, the emergence and rapid rise in insecticide resistance in malaria vectors raises many concerns about their sustainability. Therefore, the monitoring of insecticide resistance is essential for resistance management strategies implementation. We investigated the kdr mutation frequencies in 20 sympatric sites of An. arabiensis Patton, An. coluzzii Coetzee & Wilkerson and An. gambiae Giles and its importance in malaria vector control by evaluating the susceptibility to insecticides in four representative sites in Senegal. Methods: Sibling species identification and kdr mutation detection were determined using polymerase chain reaction on mosquitoes collected using pyrethrum sprays collection in 20 sites belonging to two transects with differential insecticide selection pressure. The World Health Organization (WHO) tube test was used to determine phenotypic resistance of An. gambiae s.l. to DDT, deltamethrin, lambdacyholothrin,

permethrin, bendiocarb and malathion in four representative sites. Results: The L1014F kdr mutation was widely distributed and was predominant in An. gambiae in comparison to An. arabiensis and An. coluzzii. The bioassay tests showed a general trend with a resistance to DDT and pyrethroids and a susceptibility to organophosphate and carbamate according to WHO thresholds. For deltamethrin and permethrin, the two most used insecticides, no significant difference were observed either between the two transects or between mortality rates suggesting no differential selection pressures on malaria vectors. The study of the KD times showed similar trends as comparable levels of resistance were observed, the effect being more pronounced for permethrin. Conclusions: Our study showed a widespread resistance of malaria vectors to DDT and pyrethroids and a widespread distribution of the 1014F kdr allele. These combined observations could suggest the involvement of the kdr mutation. The existence of other resistance mechanisms could not be ruled out as a proportion of mosquitoes did not harbour the kdr allele whereas the populations were fully resistant. The susceptibility to carbamate and organophosphate could be exploited as alternative for insecticide resistance management.","","","RefMan","","","","","","","","","",""
"Unknown","Unknown","Unknown","Unknown","","","2010","Norris, L. C., Norris Johns, D. E.","Insecticide resistance in the anthropophilic mosquitoes anopheles arabiensis and culex quinquefasciatus in Macha, Zambia","","83(5):51","20736582-7b5d-41a0-97e4-a8e7bf1be900","","The mosquito Anopheles arabiensis is the major vector of Plasmodium falciparum in Macha, Zambia. The arboviral and filarial vector Culex quinquefasciatus is also present in high numbers throughout the Macha region. A major portion of Zambia's current malaria control program relies on long-lasting insecticide-treated nets (LLINs) and indoor residual spraying (IRS) with insecticides. Insecticide resistance in mosquito populations has the potential to lessen and even eliminate the effectiveness of these control methods. CDC bottle bioassays and LLIN survival assays were used to characterize the An. arabiensis colony established at Macha, and this data was used as a baseline against which to compare field mosquitoes. F1 offspring of field-collected adult An. arabiensis from and Cx. quinquefasciatus from eggs collected from oviposition traps were tested for insecticide resistance. High levels of resistance to DDT, pyrethroids, malathion, and deltamethrin-treated net material were detected in Cx. quinquefasciatus, and low levels of resistance to DDT and deltamethrintreated net material were detected in An. arabiensis. Molecular assays revealed that the knock-down resistance (kdr) allele was frequent in the Cx. quinquefasciatus population, but further investigation is required to determine the level of this mutation in malaria vectors. Continued monitoring and assessment is necessary in these populations in order to determine levels of resistance and appropriately modify vector control operations.","","","RefMan","","","","","","","","","",""
"Unknown","Unknown","Unknown","Unknown","","","2015","Ojha, A., Gupta, Y. K.","Evaluation of genotoxic potential of commonly used organophosphate pesticides in peripheral blood lymphocytes of rats","Human & experimental toxicology","34(4):390-400","e3e78fba-50e7-405a-9060-46b9717c7729","","Chlorpyrifos (CPF), methyl parathion (MPT), and malathion (MLT) are among the most extensively used organophosphate (OP) pesticides in India. DNA protein cross-links (DPC) and DNA strand breaks are toxic lesions associated with the mechanism(s) of toxicity of carcinogenic compounds. In the present study, we examined the hypothesis that individual and interactive genotoxic effects of CPF, MPT, and MLT are involved in the formation of DPC and DNA strand break.

The DNA strand break was measured by comet assay and expressed as DNA damage index, while DPC estimation was carried out by fluorescence emission assay. The results showed that exposure of rat lymphocytes with CPF, MPT, and MLT caused significantly marked increase in DNA damage and DPC formation in time-dependent manner. MPT caused the highest damage, and these pesticides do not potentiate the toxicity of each other.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","2014","Ojha, A., Srivastava, N.","In vitro studies on organophosphate pesticides induced oxidative DNA damage in rat lymphocytes","Mutation research. Genetic toxicology and environmental mutagenesis","761:10-7","ef307d1c-aeea-4905-8269-1c858d6df954","","Organophosphate (OP) pesticides are widely used for agricultural and household pest control. We studied the genotoxicity of the commonly used OP pesticides chlorpyrifos (CPF), methyl parathion (MPT), and malathion (MLT), individually and in combination, in Wistar rat peripheral blood lymphocytes in vitro. DNA single-strand and double-strand breaks were measured by single cell gel electrophoresis (SCGE; comet assay). To test whether the DNA lesions were caused by oxidative stress, the DNA repair enzymes formamidoaminopyrimidineglycosylase (Fpg) and endonuclease (Endo III), which convert base damages to strand breaks, were used. Significant increases in strand breaks and in levels of the reactive oxygen species (ROS) superoxide anion and hydrogen peroxide were observed in lymphocytes treated with pesticides. MPT exposure caused the greatest DNA damage and ROS production, followed by CPF and ML. Our results demonstrate genotoxic potential of these OP pesticides.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","2013","Ojha, A., Yaduvanshi, S. K., Pant, S. C., Lomash, V., Srivastava, N.","Evaluation of DNA damage and cytotoxicity induced by three commonly used organophosphate pesticides individually and in mixture, in rat tissues","Environmental toxicology","28(10):543-52","fd8a0e32-798b-4194-92a4-90a66523c375","","Organophosphate pesticides are among the most widely used synthetic chemicals for controlling a wide variety of pests. Chlorpyrifos (CPF), methyl parathion (MPT), and malathion (MLT) are among the most extensively used organophosphate (OP) pesticides. The main target of action of OP compounds is the central and peripheral nervous system, although it has also been postulated that these compounds in both acute and chronic intoxication, disturb the redox processes and thus induce oxidative stress. The excessive generation of reactive oxygen species (ROS) causes damage to all vital macromolecules including lipids, proteins, and DNA. This study was aimed to investigate the genotoxicity and cytotoxicity of CPF, MPT, and MLT when given singly or in combination. The DNA damage was measured by alkaline single-cell gel electrophoresis or comet assay and expressed as DNA damage index. The results showed that both acute and chronic exposure with CPF, MPT, and MLT, caused significantly marked DNA damage in rat tissues namely, liver, brain, kidney, and spleen, when measured 24 hour posttreatment. It was also observed that MPT caused highest level of DNA damage and brain was maximally affected by these OP compounds. When these pesticides were given in mixture, the damage was not the sum of damage caused by individual pesticide, confirming that these pesticides do not potentiate the toxicity of each other. When the DNA damage was measured 48 and 72 hour posttreatment, the damage was partially repaired. Pesticide exposure also caused histopathological changes in rat tissues.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","1999","Osaba, L., Aguirre, A., Alonso, A., Graf, U.","Genotoxicity testing of six insecticides in two crosses of the

Drosophila wing spot test","Mutation research","439(1):49-61","839b76bb-95da-4612-a90f-56429f20604a","","Among the great variety of genotoxicity assays available, the wing spot test in Drosophila melanogaster has some characteristics that make it very suited for the screening of genotoxic activity, i.e., it is an easy and inexpensive assay using a eukaryotic organism in vivo. One of the most interesting characteristics of the assay is its capacity to detect genotoxic activity of promutagens without the necessity of an exogenous metabolic activation system. In this paper we present results obtained with a recently developed high bioactivation cross of the wing spot test (NORR cross). The positive results obtained with the five well-known procarcinogens 7, 12-dimethylbenz[a]anthracene, N-nitrosopyrrolidine, p-dimethylaminoazobenzene, diethylnitrosamine and urethane clearly show that the NORR strains are similar to the other high bioactivation strains previously described, but they lack their methodological disadvantages. We have tested six insecticides, which are characterised by having contradictory results in other genotoxicity tests, using both the standard and the high bioactivation (NORR) cross. The six insecticides analysed are the pyrethroid allethrin, the methylenedioxyphenolic compound piperonyl butoxide, the chlorinated hydrocarbons dieldrin and endrin, and the organophosphates dimethoate and malathion. We obtained negative results for all six compounds. Our results show the suitability of the wing spot test for the evaluation of compounds at the first level of genotoxicity testing.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","2009","Pan, Y., Guo, H., Gao, X.","Carboxylesterase activity, cDNA sequence, and gene expression in malathion susceptible and resistant strains of the cotton aphid, Aphis gossypii","Comparative biochemistry and physiology. Part B, Biochemistry & molecular biology","152(3):266-70","b26a6b21-13d4-4bf5-8538-15f07a21b9a8","","Levels of insecticide resistance, carboxylesterase activity, carboxylesterase expression, and the cDNA sequence of carboxylesterase gene were investigated in malathion resistant and susceptible strains of cotton aphids, Aphis gossypii (Glover). The resistant strain (MRR) exhibited 80.6-fold resistance to malathion compared to the susceptible strain (MSS) in cotton aphids. Five substrates, alpha-naphthyl acetate (alpha-NA), beta-naphthyl acetate (beta-NA), alpha-naphthyl propionate (alpha-NPr), alpha-naphthyl butyrate (alpha-NB), alpha-naphthyl caprylate (alpha-NC) and S-methyl thiobutyrate (S-MTB) were used to determine carboxylesterase activity in MRR and MSS strains of cotton aphids. Carboxylesterase activity was significantly higher in MRR strain than in MSS strain, 3.7-fold for alpha-NA, 3.0-fold for beta-NA, 2.0-fold for alpha-NPr, 2.9-fold for alpha-NB and 1.6-fold for alpha-NC, While for S-MTB, there was nearly no difference between the two strains. Two site mutations (K14Q and N354D) with high frequency were also found by sequence analysis in the MRR strain, compared with the MSS strain. The levels of gene expression for carboxylesterase of both MRR and MSS strains were determined by real-time quantitative PCRs. Compared with the MSS strain, the relative transcription levels and gene copy numbers of the carboxylesterase were 1.99- and 4.42-fold in the MRR strain, respectively. These results indicated that the increased expression of the carboxylesterase resulted from the increased transcription levels of carboxylesterase mRNA and gene copy numbers and combined with the site mutants might play role in cotton aphid resistance to malathion.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","2007","Paronetto, M. P., Achsel, T., Massiello, A., Chalfant, C. E., Sette, C.","The RNA-binding protein Sam68 modulates the alternative splicing of Bcl-x","","176(7):929-939","c704c71f-f41f-42da-b4e5-

95c9ab0646a4","","The RNA-binding protein Sam68 is involved in apoptosis, but its cellular mRNA targets and its mechanism of action remain unknown. We demonstrate that Sam68 binds the mRNA for Bcl-x and affects its alternative splicing. Depletion of Sam68 by RNA interference caused accumulation of antiapoptotic Bcl-x(L), whereas its up-regulation increased the levels of proapoptotic Bcl-x(s). Tyrosine phosphorylation of Sam68 by Fyn inverted this effect and favored the Bcl-x(L) splice site selection. A point mutation in the RNA-binding domain of Sam68 influenced its splicing activity and subnuclear localization. Moreover, co-expression of ASF/SF2 with Sam68, or fusion with an RS domain, counteracted Sam68 splicing activity toward Bcl-x. Finally, Sam68 interacted with heterogenous nuclear RNP (hnRNP) A1, and depletion of hnRNP A1 or mutations that impair this interaction attenuated Bcl-x(s) splicing. Our results indicate that Sam68 plays a role in the regulation of Bcl-x alternative splicing and that tyrosine phosphorylation of Sam68 by Src-like kinases can switch its role from proapoptotic to antiapoptotic in live cells. Â© The Rockefeller University Press.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","2013","Peterson, R. T., MacRae, C. A.","Changing the scale and efficiency of chemical warfare countermeasure discovery using the zebrafish","","10(1):e37-e42","8667aca7-c92c-4375-bee7-fcb8255fe30b","","As the number of potential chemical warfare agents grows and as the diversity of potential threat scenarios expands with nonstate actors, so a need for innovative approaches to countermeasure development has emerged. In the last few years, the utility of the zebrafish as a model organism that is amenable to high-throughput screening has become apparent and this system has been applied to the unbiased discovery of chemical warfare countermeasures. This review summarizes the in vivo screening approaches that have been used in the countermeasure discovery arena, and highlights the successes to date as well as the potential challenges in moving the field forward. Importantly, the zebrafish platform for countermeasure discovery offers a rapid response system for the development of antidotes to the continuous stream of emerging chemical warfare agents. Â© 2012 Elsevier Ltd. All rights reserved.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","1996","Pluth, J. M., Nicklas, J. A., O'Neill, J. P., Albertini, R. J.","Increased frequency of specific genomic deletions resulting from in vitro malathion exposure","Cancer research","56(10):2393-9","193b1615-4393-411d-b74f-61b8b5f39708","","Malathion is a widely used pesticide with high potential for human exposure. Epidemiological studies suggest that individuals with chronic environmental exposures to pesticides have increased risks of various hematological malignancies. The genotoxic data to date have been somewhat inconclusive with regard to malathion exposure. We have used a cell cloning assay to study the genotoxicity of in vitro exposure of human T lymphocytes to malathion. We exposed cells in G0 to doses of malathion ranging from 10 to 600 microg/ml. Mutant frequencies of treated samples showed both intra- and interindividual variability and, in some cases, slight significant increases over the controls. Molecular analysis of hprt mutants resulting from both in vitro and an in vivo malathion exposure was performed by genomic multiplex PCR. In seven in vitro experiments (using cells from four different individuals) and one experiment on an individual exposed in vivo, one or more independent mutant(s) containing a partial deletion of exon 3 have been isolated from each individual. In five of the seven mutants, the deleted regions overlap extensively, revealing an area within exon 3 exceptionally prone to deletions upon exposure to malathion, This work provides the first evidence of an association between malathion

exposure and specific mutations in human T lymphocytes. Additional work is necessary to determine the underlying molecular mechanism for these deletions and how this may relate to agricultural workers' increased risk of cancer.","","","RefMan","","","","","","","","","","Unknown","Unknown","Unknown","Unknown","","","1998","Pluth, J. M., O'Neill, J. P., Nicklas, J. A., Albertini, R. J.","Molecular bases of hprt mutations in malathion-treated human T-lymphocytes","Mutation research","397(2):137-48","bee51541-3829-4226-9212-def63edc6a4a","","Recently, we reported that 6 of 84 (7.1%) hprt mutants arising in in vitro malathion-treated human T-lymphocytes were characterized by specific genomic deletions in a 125-bp region of exon 3 (Pluth et al., Cancer Research 56 (1996) 2393-2399. We have now extended study to determine whether additional differences in molecular spectrum at a basepair level exist between control and malathion-treated mutations, and investigated whether there is evidence to support the hypothesis that malathion is an alkylating agent. We analyzed 101 hprt mutants (24 from control and 77 from treated cultures) isolated form six in vitro malathion exposures of T-lymphocytes from four healthy male donors. Analysis consisted of: Southern blotting, genomic multiplex PCR, genomic DNA sequencing and reverse transcription of PCR amplification (RT/PCR) and sequencing of the cDNA product. Mutations at several basepair sites were frequent after malathion exposure and were isolated from treated cells from at least two different individuals. Using a human hprt mutation database for comparison, the frequency of mutations at one of these sites (basepair 134) was found to be significantly elevated in the malathion-treated cell ($p < 0.0005$). Hprt mutations in malathion-treated cells arose preferentially at G:C basepairs, which is consistent with earlier reports that malathion alkylates guanine nucleotides. Assessing molecular changes at both genomic and cDNA levels in the same mutants revealed that many small, partial exon deletions (< 20 bp) in genomic DNA were often represented in the cDNA at the loss of one or more exons. In addition, It was noted that identical genomic mutations can result in different cDNA products in different T-cell isolates. These observations affirm the importance of genomic sequence analysis in combination with RT/PCR for a more accurate definition of the mutation spectrum.","","","RefMan","","","","","","","","","","Unknown","Unknown","Unknown","Unknown","","","2007","Possamai, F. P., Fortunato, J. J., Feier, G., Agostinho, F. R., Quevedo, J., Wilhelm Filho, D., Dal-Pizzol, F.","Oxidative stress after acute and sub-chronic malathion intoxication in Wistar rats","","23(2):198-204","bfb05000-3db0-4182-823b-b89199506242","","Malathion is an insecticide of the group of organophosphate pesticides (OPs), which shows strong insecticidal effects. However, it possesses mutagenic and carcinogenic properties and shows organ-specific toxicity in relation to the heart, kidney and other vertebrate organs. The exact mechanism of the genotoxic effects of malathion is not yet known. Free radical damage is an important direct or indirect factor in several pathological and toxicological processes, including malathion poisoning. The aim of the present study was the evaluation of oxidative damage in different tissues of Wistar rats, administered intra peritoneally at doses of 25, 50, 100 and 150 mg malathion/kg, after acute and sub-chronic malathion exposure. Oxidative stress evaluation was based on lipid peroxidation by levels of thiobarbituric acid reactive substances (TBARS), protein oxidation by levels of carbonyl groups, and also on the activities of superoxide dismutase and catalase, two antioxidant enzymes that detoxity superoxide radical (O2{radical dot}-) and hydrogen peroxide, respectively. The results showed that

the most sensitive targets of oxidative damage were kidney, lung and diaphragm after acute treatment, and liver, quadriceps and serum after sub-chronic treatment. Also, in general, increased lipid peroxidation measured as TBARS levels seems to be a better biomarker of oxidative stress compared to the contents of protein carbonyls after acute and sub-chronic malathion treatments. The present findings reinforce the concept that oxidative stress and particularly lipoperoxidation, are involved in OPs toxicity. Â© 2006 Elsevier B.V. All rights reserved.","","","RefMan","","","","","","","","","" "Unknown","Unknown","Unknown","Unknown","","","2014","Prathibha, Y., Murugananthkumar, R., Rajakumar, A., Laldinsangi, C., Sudhakumari, C. C., Mamta, S. K., Dutta-Gupta, A., Senthilkumaran, B.","Gene expression analysis in gonads and brain of catfish clarias batrachus after the exposure of malathion","","102:210-219","d761d728-d94c-4838-afea-10339110a8be","","Pesticides like malathion have the potential to disrupt development and reproduction of aquatic organisms including fishes. To investigate the likely consequences of malathion exposure at low doses in juvenile catfish, Clarias batrachus, we studied the expression pattern of genes encoding certain transcription factors, activin A, sex steroid or orphan nuclear receptors and steroidogenic enzymes which are known to be involved in gonadal development along with histological changes. To compare further, we also analyzed certain brain specific genes related to gonadal axis. Fifty days post hatch catfish fingerlings were exposed continuously to 1 and 10. Î¼g/L of malathion for 21 days. Results from these experiments indicated that transcript levels of various genes were altered by the treatments, which may further affect the gonadal development either directly or indirectly through brain. Histological analysis revealed slow progression of spermatogenesis in testis, while in ovary, the oil droplet oocytes were found to be higher after treatment (10. Î¼g/L). Our findings revealed that the exposure of malathion, even at low doses, hinder or modulate early gonadal development differentially by targeting gene expression pattern of transcription factors, activin A, sex steroid or orphan nuclear receptors and steroidogenic enzymes with an evidence on histological changes. Further, some of the genes showed differential expression at the level of brain in male and female sex after the exposure of malathion.","","","RefMan","","","","","","","","","" "Unknown","Unknown","Unknown","Unknown","","","2014","Qin, Q., Li, Y., Zhong, D., Zhou, N., Chang, X., Li, C., Cui, L., Yan, G., Chen, X. G.","Insecticide resistance of Anopheles sinensis and An. vagus in Hainan Island, a malaria-endemic area of China","Parasites & vectors","7:92","f0bd8550-0538-4baf-b557-7efc675a4315","","BACKGROUND: Malaria is one of the most important public health problems in Southeast Asia, including Hainan Island, China. Vector control is the main malaria control measure, and insecticide resistance is a major concern for the effectiveness of chemical insecticide control programs. The objective of this study is to determine the resistance status of the main malaria vector species to pyrethroids and other insecticides recommended by the World Health Organization (WHO) for indoor residual sprays. METHODS: The larvae and pupae of Anopheles mosquitoes were sampled from multiple sites in Hainan Island, and five sites yielded sufficient mosquitoes for insecticide susceptibility bioassays. Bioassays of female adult mosquitoes three days after emergence were conducted in the two most abundant species, Anopheles sinensis and An. vagus, using three insecticides (0.05% deltamethrin, 4% DDT, and 5% malathion) and following the WHO standard tube assay procedure. P450 monooxygenase, glutathione S-transferase and carboxylesterase activities were measured. Mutations at the knockdown resistance (kdr) gene and the ace-1 gene were detected by DNA sequencing and PCR-RFLP

analysis, respectively. RESULTS: An. sinensis and An. vagus were the predominant Anopheles mosquito species. An. sinensis was found to be resistant to DDT and deltamethrin. An. vagus was susceptible to deltamethrin but resistant to DDT and malathion. Low kdr mutation (L1014F) frequency (<10%) was detected in An. sinensis, but no kdr mutation was detected in An. vagus populations. Modest to high (45%-75%) ace-1 mutation frequency was found in An. sinensis populations, but no ace-1 mutation was detected in An. vagus populations. Significantly higher P450 monooxygenase and carboxylesterase activities were detected in deltamethrin-resistant An. sinensis, and significantly higher P450 monooxygenase, glutathione S-transferase and carboxylesterase activities were found in malathion-resistant An. vagus mosquitoes. CONCLUSIONS: Multiple insecticide resistance was found in An. sinensis and An. vagus in Hainan Island, a malaria-endemic area of China. Cost-effective integrated vector control programs that go beyond synthetic insecticides are urgently needed.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","2009","Ramphul, U., Boase, T., Bass, C., Okedi, L. M., Donnelly, M. J., Muller, P.","Insecticide resistance and its association with target-site mutations in natural populations of Anopheles gambiae from eastern Uganda","Transactions of the Royal Society of Tropical Medicine and Hygiene","103(11):1121-6","803a4a8a-7b8e-439b-879e-047227792685","","Insecticide resistance in Anopheles gambiae threatens the success of malaria vector control programmes in sub-Saharan Africa. In order to manage insecticide resistance successfully, it is essential to assess continuously the target mosquito population. Here, we collected baseline information on the distribution and prevalence of insecticide resistance and its association with target-site mutations in eastern Uganda. Anopheles gambiae s.l. adults were raised from wild-caught larvae sampled from two ecologically distinct breeding sites and exposed to WHO discriminating concentrations of DDT, permethrin, deltamethrin, bendiocarb and malathion. Survival rates to DDT were as high as 85.4%, alongside significant resistance levels to permethrin (38.5%), reduced susceptibility to deltamethrin, but full susceptibility to bendiocarb and malathion. Using molecular diagnostics, susceptible and resistant specimens were further tested for the presence of knockdown resistance (kdr) and acetylcholinesterase 1 resistance (ace-1(R)) alleles. While ace-1(R) and kdrL1014F ('kdr west') alleles were absent, the kdr L1014S ('kdr east') allele was present in both populations. In A. gambiae s.s., L1014S was closely associated with DDT and, to a lesser degree, with permethrin resistance. Intriguingly, the association between DDT resistance and the presence of L1014S is consistent with a co-dominant effect, with heterozygous individuals showing an intermediate phenotype.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","2008","Reus, G. Z., Valvassori, S. S., Nuernberg, H., Comim, C. M., Stringari, R. B., Padilha, P. T., Leffa, D. D., Tavares, P., Dagostim, G., Paula, M. M., Andrade, V. M., Quevedo, J.","DNA damage after acute and chronic treatment with malathion in rats","Journal of agricultural and food chemistry","56(16):7560-5","e412e4f8-92c2-4acc-aeb7-a9d40cbaf0b3","","Malathion is an insecticide widely used in agriculture and in public health programs that when used indiscriminately in large amounts can cause environmental pollution and risk to human health. However, it is possible that during the metabolism of malathion, reactive oxygen species can be generated, and malathion may produce oxidative stress in intoxicated rats that can be responsible for alterations in DNA molecules related in

some studies. As a result, the present study aimed to investigate the DNA damage of cerebral tissue and peripheral blood in rats after acute and chronic malathion exposure. We used single cell gel electrophoresis (Comet assay) to measure early damage in hippocampus and peripheral blood and the Micronucleus test in total erythrocytes samples. Malathion was administered intraperitoneally once a day for one day (acute) or for 28 days (chronic) protocols (in both protocols, malathion was administered at 25, 50, 100, and 150 mg/kg). Our results showed that malathion (100 and 150 mg/kg) increased the DNA damage index in the peripheral blood and in the hippocampus after both chronic and acute treatment. Malathion increased the frequency of micronuclei only in chronic treatment at 150 mg/kg dose, and induced a cytotoxic dose-dependent decrease in the frequency of polychromatic erythrocytes in the peripheral blood of rats. In conclusion, since malathion increased both the peripheral blood and hippocampus DNA damage index using the Comet assay and increased the frequency of micronuclei in the total peripheral blood, it can be regarded as a potential mutagen/carcinogenic agent.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","2010","Rezg, R., Mornagui, B., Benahmed, M., Chouchane, S. G., Belhajhmida, N., Abdeladhim, M., Kamoun, A., El-fazaa, S., Gharbi, N.","Malathion exposure modulates hypothalamic gene expression and induces dyslipedemia in Wistar rats","Food and chemical toxicology : an international journal published for the British Industrial Biological Research Association","48(6):1473-7","afd681c2-e80b-4d89-8257-f5598986a256","","Exposure to organophosphate (OP) pesticides is virtually ubiquitous. These inevitable agents are neurotoxicants, but recent evidence also points to lasting effects on carbohydrate metabolism. The aim of this study was to investigate the effects of 32 repeated treatment days with malathion, an OP insecticide, on some molecular and metabolic parameters. Malathion at 100 mg/kg was administered by gavage in Wistar rats. Results of this study indicate a significant decrease in hypothalamic corticotropin-releasing hormone mRNA, of malathion-treated rats. This result, in accordance with that of diabetic type 2 rat model, may be due to very potent negative feedback effects of glucocorticoids on hypothalamo-pituitary-adrenal (HPA) axis activity. In addition, we have recorded a significant increase in hypothalamic inducible NO synthase mRNA which probably enhances the negative feedback. These alterations are accompanied with hypertriglyceridemia that may be a favourable condition to insulin resistance. Thus, results of the present study suggest that malathion can be considered as an important risk factor in the development of diabetes type 2, which prevalence increased substantially in our country and around the world. Clearly, we need to focus further research on the specific incidences of hazardous food chemical contaminant that might be contributing to epidemic health perspectives.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","2015","Rezg, R., Mornagui, B., Santos, J. S., Dulin, F., El-Fazaa, S., Ben El-Haj, N., Bureau, R., Gharbi, N.","Protective effects of caffeic acid against hypothalamic neuropeptides alterations induced by malathion in rat","Environmental science and pollution research international","22(8):6198-207","76fe0797-0c39-4ea8-85ab-4748df3db53c","","Exposure to pesticides is suspected to cause human health problems. Our study aimed to evaluate preventive effects of caffeic acid (3,4-dihydroxycinnamic acid) in the hypothalamus against malathion-induced neuropeptides gene expression alterations. Malathion at 100 mg/kg was administered intragastrically to rats alone or in combination with caffeic acid at 100 mg/kg during 4 weeks. A molecular expression of hypothalamic neuropeptides

and plasmatic cholinesterase activity was investigated. Furthermore, we used in silico analysis, known as computational docking, to highlight the nature of acetylcholinesterase-malathion/caffeic acid interactions. Our findings showed differences in the responses and indicate that caffeic acid reversed malathion-induced decrease in corticotropin-releasing hormone mRNA but not brain-derived neurotrophic factor which presented an increased tendency. We suggest that caffeic acid can interact with acetylcholinesterase as the primary target of organophosphorus compounds. Results predict that caffeic acid can block partly the acetylcholinesterase gorge entrance via pi-pi stacking interaction with Tyr 124 and Trp 286 residues of the peripheral site leading to its stricture. Under this condition, we suggested that acetylcholine trafficking toward the catalytic site is ameliorated compared to malaoxon according to their sizes.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","1995","Riabchenko, N. I., Fesenko, E. V., Antoshchina, M. M.","[A cytogenetic analysis of the combined action of pesticides and irradiation on human lymphocytes]","Radiatsionnaia biologiia, radioecologiia / Rossiiskaia akademiia nauk","35(5):736-9","3e93179a-fc85-46b8-9c4c-8baa89ed2bc9","","The efficiency of the combined action of pesticides and irradiation at the G(o) stage was studied in cultured human lymphocytes. Carbophos (malathion) increased the yield of chromosome and chromatid fragments in irradiated lymphocytes. Herbicide 2,4-D (dichlorophenoxyacetic acid) raised lymphocyte radiosensitivity by increasing the yield of chromosome type aberrations; the radiosensitizing effect of the herbicide decreased as its concentration
increased.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","2015","Riveron, J. M., Chiumia, M., Menze, B. D., Barnes, K. G., Irving, H., Ibrahim, S. S., Weedall, G. D., Mzilahowa, T., Wondji, C. S.","Rise of multiple insecticide resistance in Anopheles funestus in Malawi: A major concern for malaria vector control","","14(1)","2ebcb1c6-24eb-4906-9625-3b947333d917","","Background: Deciphering the dynamics and evolution of insecticide resistance in malaria vectors is crucial for successful vector control. This study reports an increase of resistance intensity and a rise of multiple insecticide resistance in Anopheles funestus in Malawi leading to reduced bed net efficacy. Methods: Anopheles funestus group mosquitoes were collected in southern Malawi and the species composition, Plasmodium infection rate, susceptibility to insecticides and molecular bases of the resistance were analysed. Results: Mosquito collection revealed a predominance of An. funestus group mosquitoes with a high hybrid rate (12.2 %) suggesting extensive species hybridization. An. funestus sensu stricto was the main Plasmodium vector (4.8 % infection). Consistently high levels of resistance to pyrethroid and carbamate insecticides were recorded and had increased between 2009 and 2014. Furthermore, the 2014 collection exhibited multiple insecticide resistance, notably to DDT, contrary to 2009. Increased pyrethroid resistance correlates with reduced efficacy of bed nets (<5 % mortality by OlysetÂ® net), which can compromise control efforts. This change in resistance dynamics is mirrored by prevalent resistance mechanisms, firstly with increased over-expression of key pyrethroid resistance genes (CYP6Pa/b and CYP6M7) in 2014 and secondly, detection of the A296S-RDL dieldrin resistance mutation for the first time. However, the L119F-GSTe2 and kdr mutations were absent. Conclusions: Such increased resistance levels and rise of multiple resistance highlight the need to rapidly implement resistance management strategies to preserve the effectiveness of existing insecticide-based control

interventions.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","2015","Rocha, H. D., Paiva, M. H., Silva, N. M., de Araujo, A. P., Camacho Ddos, R., Moura, A. J., Gomez, L. F., Ayres, C. F., Santos, M. A.","Susceptibility profile of Aedes aegypti from Santiago Island, Cabo Verde, to insecticides","Acta tropica","152:66-73","657a6a2f-f198-4776-8ad9-21c1978d40c6","","In 2009, Cabo Verde diagnosed the first dengue cases, with 21,137 cases reported and Aedes aegypti was identified as the vector. Since the outbreak, chemical insecticides and source reduction were used to control the mosquito population. This study aimed to assess the susceptibility of A. aegypti populations from Santiago, Cabo Verde to insecticides and identify the mechanisms of resistance. Samples of A. aegypti eggs were obtained at two different time periods (2012 and 2014), using ovitraps in different locations in Santiago Island to establish the parental population. F1 larvae were exposed to different concentrations of insecticides (Bacillus thuringiensis var israelensis (Bti), diflubenzuron and temephos) to estimate the lethal concentrations (LC90) and calculate the respective rate of resistance (RR90). Semi-field tests using temephos-ABATE((R)) were performed to evaluate the persistence of the product. Bottle tests using female mosquitoes were carried out to determine the susceptibility to the adulticides malathion, cypermethrin and deltamethrin. Biochemical and molecular tests were performed to investigate the presence of metabolic resistance mechanisms, associated with the enzymes glutathione S-transferases (GSTs), esterases and mixed-function oxidases (MFO) and to detect mutations or alterations in the sodium channel and acetylcholinesterase genes. A. aegypti mosquitoes from Santiago exhibited resistance to deltamethrin, cypermethrin (mortality<80%) and temephos (RR90=4.4) but susceptibility to malathion (mortality>/=98%), Bti and diflubenzuron. The low level of resistance to temephos did not affect the effectiveness of Abate((R)). The enzymatic analysis conducted in 2012 revealed slight changes in the activities of GST (25%), MFO (18%), alpha-esterase (19%) and beta-esterase (17%), but no significant changes in 2014. Target site resistance mutations were not detected. Our results suggest that the A. aegypti population from Santiago is resistant to two major insecticides used for vector control, deltamethrin and temephos. To our knowledge, this is the first report of temephos resistance in an African A. aegypti population. The low level of temephos resistance was maintained from 2012-2014, which suggested the imposition of selective pressure, although it was not possible to identify the resistance mechanisms involved. These data show that the potential failures in the local mosquito control program are not associated with insecticide resistance.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","1997","Rodriguez, M. M., Bisset, J., Rodriguez, I., Diaz, C.","[Determination of insecticide resistance and its biochemical mechanisms in 2 strains of Culex quinquefasciatus from Santiago de Cuba]","Revista cubana de medicina tropical","49(3):209-14","eed73431-3b84-4000-b60a-c4bf7c4c1d5b","","It was analyzed the behavior of the resistance of 3 organophosphated insecticides (malathion, clorpirifos and methyl-pyrimifos), 3 pyrethroids (deltamethrin, lambda-cyhalothrin and cypermethrin), and 1 carbamate (propuxur) in populations of Culex quinquefasciatus from 2 municipalities of the province of Santiago de Cuba. The values of the resistance factor proved that there is resistance to malathion and clorpirifos. However, in spite of the existence of a high frequency of the mechanisms of elevated esterases and altered acetylcholinesterase no resistance to methylpymirifos, was observed which demonstrated that this insecticide is not affected

by these mechanisms selected in our populations of Culex quinquefasciatus. There was resistence to deltamethrin, and lambda-cyhalothrin in Santiago de Cuba, whereas it was moderate to cypermethrin in Santiago and San Luis. Resistance to deltamethrin was also found in San Luis, but it was mild to lambda-cyhalothrin. The results obtained from the use of the synergists S,S,S tributyl phosphotritiade (DBF) and piperonyl butoxide (PB) indicated that the mechanisms of resistance of unspecific esterases and oxidases of multiple function are involved in the resistance to pyrethroids in both strains from Santiago de Cuba and San Luis. It was determined by the biochemical tests that there existed a high frequency of the mechanisms of esterases and altered acetylcholinesterase. The results of the polyacrylamide gel electrophoresis (PAGE) showed that esterase B1 appears more frequently associated with esterases A6 and B6. It was inferred that this association could be connected with the resistance to pyrethroids.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","1999","Rodriguez-Ariza, A., Alhama, J., Diaz-Mendez, F. M., Lopez-Barea, J.","Content of 8-oxodG in chromosomal DNA of Sparus aurata fish as biomarker of oxidative stress and environmental pollution","Mutation research","438(2):97-107","e255847a-ee9c-4f55-88c6-421b337c9277","","The 8-oxodG content has been measured in chromosomal DNA of gilthead seabream (Sparus aurata) by HPLC-EC. Susceptibility of different tissues to oxidative DNA damage was studied by exposing fish to model pollutants. Cu(II), paraquat (PQ) and malathion failed to promote DNA oxidation in liver, while dieldrin significantly increased the 8-oxodG content in this organ, but not in gills or blood. After PQ exposure, fish liver showed high levels of glucose-6-P dehydrogenase (G-6PDH) and GSSG reductase activities. The increased antioxidant status and the lack of a specific transport system could explain the lack of susceptibility of liver to DNA oxidative damage induced by PQ. Increased levels of 8-oxodG were detected in the gills of PQ-exposed fish after 8 and 24 h. In contrast, after 48 h exposed fish contained lower 8-oxodG levels than controls. The existence of a PQ transport system in this O2-rich organ and the lack of a significant increase in antioxidant defenses would explain the sensitivity of gills to DNA damage promoted by PQ. Elimination of this soluble chemical and the putative induction of DNA-repair enzymes specific for oxidative damages could explain the drop of 8-oxodG levels at longer times. Fish exposed to moderate levels of urban and industrial pollution showed significantly high 8-oxodG content in hepatic DNA. We conclude that 8-oxodG determination in chromosomal DNA by HPLC-EC is a potentially useful biomarker of environmental pollution, although its response is still somewhat lower than that of other well-established biomarkers of oxidative stress.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","1995","Rodriguez-Ariza, A., Diaz-Mendez, F. M., Navas, J. I., Pueyo, C., Lopez-Barea, J.","Metabolic activation of carcinogenic aromatic amines by fish exposed to environmental pollutants","Environmental and molecular mutagenesis","25(1):50-7","90ef45f3-cace-4df3-ac10-1b7232ef44f5","","Activation of arylamines to mutagenic metabolites by hepatic S9 fractions has been evaluated as a biomaker of fish exposure to pollutants, using gilthead seabream (Sparus aurata), a valuable fish species from the Spanish South Atlantic littoral, as model organism. To obtain maximal sensitivity to the mutagenic action of aromatic amines, a strain of Salmonella typhimurium overproducing O-acetyltransferase was used. Fish were treated with Aroclor 1254, pesticides (malathion and dieldrin), or copper(II), and compared to Aroclor 1254-treated rats. The promutagen

activation capabilities of the S9 fractions were further characterized by studying the effect of two monooxygenase inhibitors, alpha-naphthoflavone, a well known inhibitor of aromatic hydrocarbon-inducible forms of cytochrome P450, and methimazole, a substrate for the flavin monooxygenase (FMO) system. This study shows that 2-aminoanthracene (2-AA) and 2-acetylaminofluorene (AAF) activation by gilthead liver is enhanced by treatment of fish with different xenobiotics. The catalyst responsible for this enhanced activation appears to be different for each promutagen and, at least for 2-AA, dependent on the type of xenobiotic. The data presented indicate further that treatment of gilthead with some compounds, such as malathion and dieldrin, enhances the activation of aromatic amines in liver, without inducing ethoxyresorufin-O-deethylase activity. The use of acetyltransferase-overproducing bacteria appears to be a useful tool in the study of arylamine activation by fish liver, where biotransformation capability is lower than in mammals.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","2007","Salazar, Z., Ducolomb, Y., Betancourt, M., Bonilla, E., Cortes, L., Hernandez-Hernandez, F., Gonzalez-Marquez, H.","Gene expression analysis on the early development of pig embryos exposed to malathion","International journal of toxicology","26(2):143-9","5f63cad5-f36d-4756-b7ed-d6e7ae6acd9c","","Malathion is a widely used pesticide and there is evidence that it could alter mammal's germ and somatic cells, as well as cell lines. There are not enough studies showing how the nonacute malathion doses affect gene expression. This study analyzes gene expression alterations in pig morular embryos exposed in vitro, for 96 h, to several malathion concentrations after in vitro fertilization. cDNA libraries of isolated morular embryos were created and differential screenings performed to identify target genes. Seven clones were certainly identified. Genes related to mitochondrial metabolism as cytochrome c subunits I and III, nuclear genes such as major histocompatibility complex I (MHC I), and a hypothetical protein related with a splicing factor were the target of malathion's deregulation effect. The widespread use of malathion as a pesticide should be regarded with reproductive implications and more detailed analysis would yield more about molecular mechanisms of malathion injury on embryo cells.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","2012","Samb, B., Wondji, C. S., Dia, I., Konate, L., Faye, O.","First evidence of pyrethroid resistance in an anopheles funestus population from senegal","","87(5):218","354d5bee-a70d-41c3-86a2-accbe9841579","","Anopheles funestus is one of the major malaria vectors in tropical Africa notably in Senegal. The highly anthropophilic and endophilic behaviours of this mosquito make it a good target for vector control operations through the use of insecticide treated nets, long-lasting insecticide nets and indoor residual spraying. However, little is known about the resistance status to insecticides of field populations of this vector in Senegal and the potential underlying resistance mechanisms. To fill this gap in our knowledge, we assessed the susceptibility status of An. funestus populations from Gankette Balla, located in the Senegal River Basin. WHO bioassays indicated that An. funestus in Gankette is resistant to lambda-cyhalothrin 0.05% (74.32% mortality / n = 222). Suspected resistance was observed to deltamethrin 0.05% (87.72% mortality / n = 114), permethrin 0.75% (91.37% mortality / n = 139), DDT 4% (93.20% mortality / n = 147), bendiocarb 0.1% (94.27% mortality / n = 157) and dieldrin 4% (96.41% mortality / n = 306). However this population is fully susceptible to malathion 5 % (100% mortality / n = 50) and fenitrothion 1% (100% mortality / n = 55). Sequencing of the fragments of Voltage- Gated Sodium Channel did not detect the

L1014F mutation. A microarray analysis indicated that the lambda-cyhalothrin resistance in Gankette is conferred by metabolic resistance mechanism under the control of P450 genes. This study represents the first report of pyrethroid resistance in An. funestus from Senegal. These findings should be taken into account by malaria control programs and further studies are needed to establish the geographic distribution of this resistance across Senegal.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","2014","Samb, B., Wondji, C. S., Dia, I., Konate, L., Faye, O.","Investigating the mechanisms of DDT and dieldrin resistance in field population of anopheles funestus in Senegal","","91(5):231-232","534507a2-810b-4823-97c7-7b582529632f","","Insecticide resistance in Anopheles funestus, one of the main malaria vectors, is threatening malaria control in Africa. Elucidation of the mechanisms of resistance is crucial to the design of suitable resistance management strategies. Therefore, we have investigated the mechanisms responsible for DDT and dieldrin resistance in An. funestus population from Senegal. Insecticide susceptibility assays were carried out using 2-5 day old F1 adults generated from indoor-collected, blood-fed female of An. funestus from Gankette, in Northern Senegal. WHO bioassays indicated that An. funestus is resistant to lambda-cyhalothrin 0.05% (74.64% mortality / n = 222), DDT 4% (83.36% mortality / n = 158) and deltamethrin 0.05% (88.53% mortality / n = 114). Suspected resistance was observed to permethrin 0.75% (91.19% mortality / n = 139), bendiocarb 0.1% (94.13% mortality / n = 157) and dieldrin 4% (96.41% mortality / n = 306). However this population is fully susceptible to malathion 5 % (100% mortality / n = 50) and fenitrothion 1% (100% mortality / n = 55). Genome-wide transcription analysis using microarray and quantitative RT-PCR revealed that the cytochrome P450 CYP6M7 was the detoxification gene most commonly over-expressed in DDT resistant mosquitoes and field unexposed to insecticide compared to a laboratory susceptible strain. In addition, several others genes with diverse functions including glutathione S-transferases were also overexpressed. Using the pyro-sequencing method, The A296S Rdl(R) target site mutation was detected in all dieldrin resistant mosquitoes but at a low frequency (14%) in the field sample. Our study has revealed a strong association between the dieldrin resistance phenotype and the presence of the Rdl mutation. TaqMan genotyping revealed that the L119F mutation in the GSTe2 gene conferring DDT resistance in Benin is completely absent in Senegal. This indicates a shift of DDT resistance mechanisms in West Africa An. funestus. These results could help to guide the implementation of suitable control interventions against this vector in Senegal.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","2013","Sanabrais, M. A., Navarrete-Meneses, M. P., Betancourt, M., Salas-LabadÃ-a, C.","ETV6 and RUNX1 aberrations produced by exposure to permethrin and malathion on human lymphocytes in vitro. pÃ©rez-vera p1","","54:S44","9421aca5-79fe-43fd-b261-25b5acec7732","","Introduction: Acute Lymphoblastic Leukemia (ALL) is the most frequent cancer in childhood with multifactorial etiology, including exposure to pesticides. Although numerous epidemiological studies associate ALL with the use of insecticides, there is limited biological evidence to support it. ALL blasts frequently present acquired abnormalities in ETV6 and RUNX1 genes, associated to the origin and evolution of the disease. The aim of this study was to detect alterations in ETV6 and RUNX1 induced by permethrin and malathion on human lymphocytes in vitro. Methods: Lymphocytes from two male healthy volunteers were cultured for 72h and exposed to 200mM of permethrin or malathion for the last 24h. Solvents were used as negative controls. ETV6 and RUNX1 genes were

analyzed in 1000 nuclei by fluorescence in situ hybridization (FISH). Results: For both insecticides, cells with copy number deviations were observed more frequently (94%: -/+ETV6, - RUNX1) than structural aberrations (6%: ETV6-RUNX1 fusion; amplification). With both agents, the number of cells with numerical aberrations was increased, but only the treatment with permethrin showed statistical difference ($p<0.01$). Discussion: Numerical deviations of ETV6 and RUNX1 were observed by malathion and permethrin exposure. Permethrin caused the major difference; the numerical abnormalities observed could be originated by an aneuploidogenic effect, although the origin of these abnormalities must be explored. These insecticides induced numerical and structural abnormalities which are commonly detected in lymphoblast of ALL-patients with active disease, suggesting a possible contribution to the development of this leukemia.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","2014","Santos, S. A., Fermino, F., Moreira, B. M., Araujo, K. F., Falco, J. R., Ruvolo-Takasusuki, M. C.","Critical electrolyte concentration of silk gland chromatin of the sugarcane borer Diatraea saccharalis, induced using agrochemicals","Genetics and molecular research : GMR","13(3):7958-64","1aad49fe-aa96-4a04-a52e-5250eaf96680","","The sugarcane borer Diatraea saccharalis is widely known as the main pest of sugarcane crop, causing increased damage to the entire fields. Measures to control this pest involve the use of chemicals and biological control with Cotesia flavipes wasps. In this study, we evaluated the insecticides fipronil (Frontline; 0.0025%), malathion (Malatol Bio Carb; 0.4%), cipermetrina (Galgotrin; 10%), and neem oil (Natuneem; 100%) and the herbicide nicosulfuron (Sanson 40 SC; 100%) in the posterior region silk glands of 3rd- and 5th-instar D. saccharalis by studying the variation in the critical electrolyte concentration (CEC). Observations of 3rd-instar larvae indicated that malathion, cipermetrina, and neem oil induced increased chromatin condensation that may consequently disable genes. Tests with fipronil showed no alteration in chromatin condensation. With the use of nicosulfuron, there was chromatin and probable gene decompaction. In the 5th-instar larvae, the larval CEC values indicated that malathion and neem oil induced increased chromatin condensation. The CEC values for 5th-instar larvae using cipermetrina, fipronil, and nicosulfuron indicated chromatin unpacking. These observations led us to conclude that the quantity of the pesticide does not affect the mortality of these pests, can change the conformation of complexes of DNA, RNA, and protein from the posterior region of silk gland cells of D. saccharalis, activating or repressing the expression of genes related to the defense mechanism of the insect and contributing to the selection and survival of resistant individuals.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","2010","Schofield, D. A., Dinovo, A. A.","Generation of a mutagenized organophosphorus hydrolase for the biodegradation of the organophosphate pesticides malathion and demeton-S","Journal of applied microbiology","109(2):548-57","133d5d9a-d5da-48f6-8ce6-c12b017a9032","","AIMS: The bacterial organophosphorus hydrolase (OPH) enzyme hydrolyses and detoxifies a broad range of toxic organophosphate pesticides and warfare nerve agents by cleaving the various phosphorus-ester bonds (P-O, P-F, P-CN, P-S); however, OPH hydrolyses these bonds with varying efficiencies. The aim of this study was to generate a variant OPH enzyme with improved hydrolytic efficiency against the poorly hydrolysed P-S class of organophosphates. METHODS AND RESULTS: The gene encoding OPH was sequentially mutated at specific codons by saturation mutagenesis and screened for improved activity against

the P-S substrates demeton-S methyl and malathion. Escherichia coli lysates harbouring the variants displayed up to 177- and 1800-fold improvement in specific activity against demeton-S methyl and malathion, respectively, compared to the wild-type lysates. The specificity constants of the purified variant proteins were improved up to 25-fold for demeton-S methyl and malathion compared to the wild-type. Activity was associated with organophosphate detoxification as the hydrolysed substrate lost the ability to inhibit acetylcholinesterase. The improved hydrolytic efficiency against demeton-S translated to the improved ability to hydrolyse the warfare agent VX. CONCLUSIONS: OPH variant enzymes were generated that displayed significantly improved ability to hydrolyse and detoxify organophosphates harbouring the P-S bond. SIGNIFICANCE AND IMPACT OF THE STUDY: The long-term goal is to generate an environmentally-friendly enzyme-mediated bioremediation approach for the removal of toxic organophosphate compounds in the environment.","","","RefMan","","","","","","","","","","Unknown","Unknown","Unknown","Unknown","","","2013","Serrano, R. M., Camargo, D. G., Cochero, S., Vergara, E. M., Lacouture, H. S., Rivadeneira, Z. F., Torres, M., Olaya, S. G., Perdomo, E., Silva, B. G., Flores, A. E.","Characterization of insecticides resistance in aedes aegypti population from the caribbean region of Colombia","","89(5):410","4c359627-19ac-41f1-aff9-654343e5f2fb","","We determined the susceptibility to insecticides and biochemical and molecular mechanisms involved in insecticide resistance of nine populations of Aedes aegypti in the Caribbean Region of Colombia. Bioassays were performed for temephos in larvae according to WHO and bottle bioassays for adults with the insecticides: lambdacyalothrin, cyfluthrin, permethrin, deltamethrin, malathion, fenitrothion and pirimiphos-methyl The resistance ratios were calculated using the susceptible Rockefeller strain as a control. Additionally, the organochloride DDT was evaluated through the impregnated papers technique. Biochemical resistance mechanism were identified associated with high level of Î±, Î²-esterases, mixed-function oxidases, insensitive acetylcholinesterase and glutathione S-transferases; we identified the mutation Ile1,016 in the gene of the voltage-dependent sodium channel and its frequency. All populations were susceptible to the organophosphates evaluated (RR=1x-4x) with exception of Puerto Colombia and Soledad (AtlÃ¡ntico) strains which demonstrated high and moderate resistance to temephos (RR=15x) and (RR=5x), respectively and Sincelejo (Sucre) with moderate resistance to pirimiphos-methyl (RR=5x). All populations were resistant to DDT (2-28% mortality). Strains evaluated exhibited values of resistance to lambda-cyalothrin between 4,9-83 fold, for deltamethrin between 0,9-37,8 fold, cyfluthrin with 0,5-33,8 fold and permethrin of 1,8 -17,9 fold. Over-expression of glutathione S-transferases were found in all populations with the exception of Puerto Colombia (AtlÃ¡ntico) and Cartagena (Bolivar); as well as Î±-esterase in strains: Valledupar (Cesar) and Monteria (Cordoba); and insensitive acetylcholinesterase in Puerto Colombia strain (Atlantico). The mutation Ile1,016 was registered in all populations with variability in its frequency.","","","RefMan","","","","","","","","","","Unknown","Unknown","Unknown","Unknown","","","2014","Shang, Q., Pan, Y., Fang, K., Xi, J., Wong, A., Brennan, J. A., Cao, C.","Extensive Ace2 duplication and multiple mutations on Ace1 and Ace2 are related with high level of organophosphates resistance in Aphis gossypii","Environmental toxicology","29(5):526-33","3a89088b-bf65-4be0-b246-4d8b6e07453c","","Aphis gossypii (Glover) has been found to possess multiple mutations in the acetylcholinesterase (AChE) gene (Ace) that might involve target site

insensitivity. In vitro functional expression of AChEs reveals that the resistant Ace1 (Ace1R) and Ace2 (Ace2R) were significantly less inhibited by eserine, omethoate, and malaoxon than the susceptible Ace1 (Ace1S) and Ace2 (Ace2S). Furthermore, in both the mutant and susceptible AChEs, Ace2 was significantly less sensitive to eserine, omethoate, and malaoxon than Ace1. These results suggested that both the mutant Ace1 and Ace2 were responsible for omethoate resistance, while the mutant Ace2 played a major role in insecticide resistance. The DNA copy number and transcription level of Ace2 were 1.52- and 1.88-fold higher in the ORR strain than in the OSS strain. Furthermore, the DNA copy number and transcription level of Ace2 were significantly higher than that of Ace1 in either OSS or ORR strains, demonstrating the involvement of Ace2 gene duplication in resistance. Thus, the authors conclude that omethoate resistance in cotton aphids appears to have evolved through a combination of multiple mutations and extensive Ace2R gene duplication.","","","RefMan","","","","","","","","","","Unknown","Unknown","Unknown","Unknown","","","2014","Singh, R. B., Adak, T., Kapoor, N., Singh, O. P.","Widespread emergence of pyrethroid resistance and presence of knock down resistance (Kdr) mutations in Indian Aedes Aegypti populations","","91(5):40","da99a995-c237-4f8b-b7d0-8bb11eedb824","","Aedes aegypti, primary vector of yellow fever in Americas, is the primary vector for dengue and chikungunya in India. Resistance to DDT, temephos, permethrin and deltamethrin has been reported in this species in America, Brazil, China, Thailand, Indonesia, Vietnam and many other tropical and subtropical countries; however there is scanty information about insecticide resistance of this species in Indian populations. We collected immature of Ae. aegypti from different geographical regions of India; Haryana, Bangalore, Chennai, West Bengal, Bhopal and Khandwa. Larvae/ pupae were allowed to emerge into adults. WHO standard insecticide susceptibility tests for DDT (4%), permethrin (0.75%) and deltamethrin (0.05%) were carried out on 2-3 days old adult females. We found varying susceptibility for different insecticides in different populations. Very high level of resistance against DDT was observed in Kolkata population (12.07% mortality) moderate resistance in Bangalore, Chennai and Haryana (55.13% - 66.16% mortality) and incipient resistance in Bhopal and Khandwa populations (91.11% mortality). Deltamethrin resistance was found to be moderate level in Bangalore, Chennai, (48.48% - 80.83% mortality) and low level in Bhopal, Kolkata and Haryana (82.48% - 83.58% mortality). Permethrin was still effective in most of the population showing moderate level of resistance Kolkata population (74.29 % mortality) and low level in Bangalore, Chennai, Haryana and Bhopal populations (92.31% - 98.37% mortality). Two populations (Haryana and Kolkata) tested for Malathion were found susceptible (100% mortality). Here we also studied a knock down resistance (kdr) mutation reported worldwide F1534C and found it few populations. This mutation was absent in Bangalore, Chennai, Khandwa and Bhopal populations. In Haryana population the frequency for mutant allele is very low 0.095 but the high degree of resistance in Kolkata population can be correlated to the high frequency of mutant allele 0.48. Resistance against pyrethroids is alarming and has negative effect on the success of pyrethroid based personal protection methods. Understanding of resistance mechanism is helpful for effective vector control strategies.","","","RefMan","","","","","","","","","","Unknown","Unknown","Unknown","Unknown","","","2011","Singh, S., Kumar, V., Thakur, S., Banerjee, B. D., Chandna, S., Rautela, R. S., Grover, S. S., Rawat, D. S., Pasha, S.

T., Jain, S. K., Ichhpujani, R. L., Rai, A.","DNA damage and cholinesterase activity in occupational workers exposed to pesticides","Environmental toxicology and pharmacology","31(2):278-85","df8824fc-6565-4127-beb4-f60e169925e8","","The present study was designed to evaluate genotoxicity, acetyl cholinesterase (AChE) activity, hepatic and renal toxicity in occupational workers exposed to mixture of pesticides (n=70) with same number of healthy subjects as controls. The mean comet tail DNA % (TD %) and tail moment (TM) were used to measure DNA damage, while AChE activity and other biochemical parameters such as markers of nephrotoxicity (urea and creatinine) and hepatotoxicity (AST, ALT and ALP) were measured as biomarkers for toxicity due to exposure of pesticides. The occupational workers were continuously exposed to mixture of pirimiphos methyl, chlorpyrifos, temephos and malathion on a regular interval as per usage and activity. The comet assay using lymphocytes of exposed workers showed significantly higher TD percentage value (60.43% vs. 31.86%, p<0.001) and TM value (14.48 mum vs. 6.42 mum, p<0.001) in occupational workers as compared to controls. AChE activity in erythrocytes was found to be decreased (3.45 KAU/L vs. 9.55 KAU/L in controls, p<0.001) and associated with the duration of exposure to pesticides used by the workers. Enzyme levels for hepatic and renal functions were also found significantly different in occupational workers than healthy controls (p<0.001). These results suggest that the exposure to mixture of pirimiphos methyl, chlorpyrifos, temephos and malathion may induce DNA damage, decrease in AChE activity, hepatotoxicity as well as nephrotoxicity. Periodic biomonitoring of these biomarkers along with imparting education and training to occupational workers for safe application of pesticides is recommended for its potential hazards.","","","RefMan","","","","","","","","",""
"Unknown","Unknown","Unknown","Unknown","","","2014","Sirotkina, M., Efremenko, E. N.","Rhodococcus lactonase with organophosphate hydrolase (OPH) activity and His6-tagged OPH with lactonase activity: Evolutionary proximity of the enzymes and new possibilities in their application","","98(6):2647-2656","ab8640f0-1caa-4583-aab7-f188b1f0d4cf","","Decontamination of soils with complex pollution using natural strains of microorganisms is a matter of great importance. Here we report that oil-oxidizing bacteria Rhodococcus erythropolis AC-1514D and Rhodococcus ruber AC-1513D can degrade various organophosphorous pesticides (OP). Cell-mediated degradation of five different OP is apparently associated with the presence of N-acylhomoserine lactonase, which is pronouncedly similar (46-50 %) to the well-known enzyme organophosphate hydrolase (OPH), a hydrolysis catalyst for a wide variety of organophosphorous compounds. Additionally, we demonstrated the high lactonase activity of hexahistidine-tagged organophosphate hydrolase (His6-OPH) with respect to various N-acylhomoserine lactones, and we determined the catalytic constants of His6-OPH towards these compounds. These experimental data and theoretical analysis confirmed the hypothesis about the evolutionary proximity of OPH and lactonases. Using Rhodococcus cells, we carried out effective simultaneous biodegradation of pesticide paraoxon (88 mg/kg) and oil hydrocarbon hexadecane (6.3 g/kg) in the soil. Furthermore, the discovered high lactonase activity of His6-OPH offers new possibilities for developing an efficient strategy of combating resistant populations of Gram-negative bacterial cells. Â© 2013 Springer-Verlag.","","","RefMan","","","","","","","","",""
"Unknown","Unknown","Unknown","Unknown","","","2000","Smyth, K. A., Boyce, T. M., Russell, R. J., Oakeshott, J. G.","MCE activities and malathion resistances in field populations of the australian sheep blowfly (Lucilia cuprina)","Heredity","84 (Pt

1):63-72","fd8f4ac8-cef6-4ac7-bb16-eef210f627e0","","Malathion resistance has been shown to be the result of a single point mutation in the LcalphaE7 gene in four independently isolated chromosomes of Lucilia cuprina. The resultant amino acid substitution specifies high malathion carboxylesterase (MCE) activity. We have assayed MCE activities and resistance to malathion in three sets of field-derived samples, two sets of isogenic lines and five mass populations, and show that resistance to malathion in these samples is associated with high MCE activity in both sets of isogenic lines and four of the five mass populations. Additional mechanisms contributing to MCE activity or malathion resistance may be present in one of the mass populations. A second point mutation in LcalphaE7 is responsible for conferring diazinon resistance by encoding an increased organophosphate (OP) hydrolase activity. We also assayed diazinon resistances from the same three samples and show that diazinon and malathion resistances were in complete disequilibrium, with two exceptions. One exception involves the mass population with additional resistance mechanism(s) and the other involves three isogenic lines that are resistant to both insecticides. The molecular data for these lines suggest that they carry a duplication of the LcalphaE7 gene.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","2014","Sparling, D. W., Bickham, J., Cowman, D., Fellers, G. M., Lacher, T., Matson, C. W., McConnell, L.","In situ effects of pesticides on amphibians in the Sierra Nevada","","24(2):262-278","a2e28ec0-03c6-463d-b914-654dfd0a15f6","","For more than 20Â years, conservationists have agreed that amphibian populations around the world are declining. Results obtained through laboratory or mesocosm studies and measurement of contaminant concentrations in areas experiencing declines have supported a role of contaminants in these declines. The current study examines the effects of contaminant exposure to amphibians in situ in areas actually experiencing declines. Early larval Pseudacris regilla were translocated among Lassen Volcanic, Yosemite and Sequoia National Parks, California, USA and caged in wetlands in 2001 and 2002 until metamorphosis. Twenty contaminants were identified in tadpoles with an average of 1.3â€"5.9 (maximumÂ =Â 10) contaminants per animal. Sequoia National Park, which had the greatest variety and concentrations of contaminants in 2001, also had tadpoles that experienced the greatest mortality, slowest developmental rates and lowest cholinesterase activities. Yosemite and Sequoia tadpoles and metamorphs had greater genotoxicity than those in Lassen during 2001, as determined by flow cytometry. In 2001 tadpoles at Yosemite had a significantly higher rate of malformations, characterized as hemimelia (shortened femurs), than those at the other two parks but no significant differences were observed in 2002. Fewer differences in contaminant types and concentrations existed among parks during 2002 compared to 2001. In 2002 Sequoia tadpoles had higher mortality and slower developmental rates but there was no difference among parks in cholinesterase activities. Although concentrations of most contaminants were below known lethal concentrations, simultaneous exposure to multiple chemicals and other stressors may have resulted in lethal and sublethal effects.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","2016","Taskin, B. G., Dogaroglu, T., Kilic, S., Dogac, E., Taskin, V.","Seasonal dynamics of insecticide resistance, multiple resistance, and morphometric variation in field populations of Culex pipiens","Pesticide biochemistry and physiology","129:14-27","1f00220f-6d67-4e53-ac7e-39f32e4f7c85","","Resistance to insecticides that impairs nervous transmission has been widely investigated in mosquito populations as insecticides are crucial to effective

insect control. The development of insecticide resistance is also of special interest to evolutionary biologists since it represents the opportunity to observe the genetic consequences of a well-characterized alteration in the environment. Although the frequencies of resistance alleles in Culex pipiens populations against different groups of insecticides have been reported, no detailed information is available on the relative change in these allele frequencies over time. In this study, we collected mosquitoes of the Cx. pipiens complex from six locations in three seasons in the Aegean region of Turkey and examined the i) seasonal variations in resistance to four different chemical classes of insecticides, ii) seasonal fluctuations in frequencies of resistance-associated target-site mutations of the three genes (ace-1, kdr, and Rdl), and iii) potential seasonal variations in wing morphometric characters that may be modified in resistant mosquitoes. Our bioassay results indicated the presence of different levels of resistance to all tested insecticides for all three seasons in all locations. The results of the PCR-based molecular analysis revealed low frequencies of mutations in ace-1 and Rdl that are associated with resistance to malathion, bendiocarb, and dieldrin and no obvious seasonal changes. In contrast, we detected high frequencies and striking seasonal changes for two kdr mutations associated with resistance to DDT and pyrethroids. In addition, the evaluation of the field populations from all seasons in terms of the combinations of polymorphisms at four resistance-associated mutations did not reveal the presence of insects that are resistant to all pesticides. Results from the morphological analysis displayed a similar pattern for both wings and did not show a clear separation among the samples from the three different seasons. The results of this study have advanced our knowledge of the potential dynamics of insecticide resistance among populations of the Cx. pipiens complex. The implications of these results to the understanding of the evolution of insecticide resistance and the management of resistance in mosquitoes are discussed.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","2007","Tisch, M., Faulde, M., Maier, H.","[Genotoxic effects of insecticides in current use on mucosal epithelial cells from human tonsil tissue]","Hno","55 Suppl 1:E15-22","2db433c4-54f3-45a8-9d76-3d675a8544c8","","BACKGROUND: Vector control is of critical medical importance in disease prevention, as reflected in sections 17 and 18 of the German Protection Against Infection Act. In the past, a large number of biocides were found to be hazardous to human health and were banned from the market, subsequently being replaced by new active ingredients and galenic forms. Many of these new insecticides are available in spray or nebuliser form. Whether these preparations have genotoxic effects on mucosal epithelial cells of the upper aerodigestive tract has thus far not been investigated. MATERIALS AND METHODS: We used the comet assay, as a well-established genotoxicity test, to investigate whether malathion, diazinon, pyridostigmine bromide, piperonyl butoxide, silafluofen, and fipronil had genotoxic effects on tonsil specimens taken from 85 patients. RESULTS: All substances tested proved to have a strong genotoxic effect on mucosal epithelial cells taken from human tonsil tissue. We found clear differences between substance groups. CONCLUSIONS: Sufficient doses of a wide range of insecticides are indispensable in many areas of human life, especially for the prevention of diseases. Depending on the method of application, however, ingestion or inhalation of these substances can damage mucosal epithelial cells of the upper aerodigestive tract. Further epidemiological studies should be undertaken to investigate whether this involves potential health hazards in at-risk

populations.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","1997","Titenko-Holland, N., Windham, G., Kolachana, P., Reinisch, F., Parvatham, S., Osorio, A. M., Smith, M. T.","Genotoxicity of malathion in human lymphocytes assessed using the micronucleus assay in vitro and in vivo: a study of malathion-exposed workers","Mutation research","388(1):85-95","9941ac26-d411-4ecd-8998-6986b9622876","","The aerial application of malathion, a widely used organophosphate insecticide, has raised public concerns about potential adverse health effects. We therefore studied micronucleus formation in human lymphocytes as a biomarker of genotoxicity both in vitro and in vivo. Lymphocytes were cultured either as whole blood or after Ficoll isolation and treated with malathion in doses from 5 to 100 micrograms/ml for 48 h. A significant increase in micronucleated cells (47.5/1000 versus 16.0/1000 in DMSO control, $p < 0.001$) was found in isolated lymphocytes at high dose levels (75-100 micrograms/ml), concurrent with cytotoxicity and a strong inhibition of proliferation ($p < 0.001$). Many of the treated cells also possessed multiple micronuclei. Antikinetochore-antibody staining revealed that the majority of malathion-induced micronuclei were kinetochore-negative. A significant dose-response was also observed in whole blood cultures, although the increase in micronucleated cells was lower than in isolated lymphocyte cultures ($p = 0.03$). When the same technique was applied to lymphocytes of 38 intermittently malathion-exposed workers involved in the Mediterranean Fruit Fly Eradication Program in California, no change in either proliferation or micronucleus level was observed compared with an unexposed control group. We conclude that malathion has a relatively low potential to cause chromosome damage in vitro, and corresponding doses are much higher than ones that even professional applicators are likely to be exposed to in vivo. The potential risk of chromosome damage for malathion exposure in vivo is therefore relatively low. More studies are needed to assess the possibility of interaction of malathion with other pesticides through combined exposure.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","2004","Tuschl, H., Schwab, C. E.","Flow cytometric methods used as screening tests for basal toxicity of chemicals","Toxicology in vitro : an international journal published in association with BIBRA","18(4):483-91","0690ab81-6ba7-487d-8df9-87d196cd4b22","","Aim of the present study was to evaluate the suitability of flow cytometry to test in vitro effects of toxicants. Flow cytometry offers the possibility to study several parameters simultaneously, e.g. cell cycle modulation, apoptosis and necrosis within the same cell culture. The effects of six compounds (acetaminophen=AAP, isoniazid=INH, digoxin, malathion, paraquat and 2,4-dichlorophenoxy acetic acid=2,4-D) on cell cycle were investigated in HepG2 cells and the induction of apoptosis/necrosis was analyzed by a spectrum of flow cytometric assays in HepG2, AAH-1 and YAC-1 cells. Early indicators of apoptosis--loss of mitochondrial membrane polarization--as well as later events of the apoptotic process--annexin V binding and DNA fragmentation--were studied. The phases of the cell cycle and the occurrence of a sub-G(0) peak of apoptotic cells were determined with propidium iodide staining. The present investigation demonstrated good correlations between results obtained by flow cytometric analyses and the IC50 data of the MEIC (=Multicenter Evaluation of In Vitro Cytotoxicity) study. Regarding the short time required for the tests, the possibility of investigating several parameters of cytotoxicity simultaneously and the ease of performance, flow cytometric analyses are well suited for the pre-screening for toxic effects of chemicals.","","","RefMan","","","","","","","","","",""

"Unknown","Unknown","Unknown","Unknown","","","2016","Varona-Uribe, M. E., Torres-Rey, C. H., Diaz-Criollo, S., Palma-Parra, R. M., Narvaez, D. M., Carmona, S. P., Briceno, L., Idrovo, A. J.","Exposure to pesticide mixtures and DNA damage among rice field workers","Archives of environmental & occupational health","71(1):3-9","398f2f79-8130-4445-b872-8eb0e4c693e2","","This study describes the use of pesticides mixtures and their potential association with comet assay results in 223 rice field workers in Colombia. Thirty-one pesticides were quantified in blood, serum, and urine (15 organochlorines, 10 organophosphorus, 5 carbamates, and ethylenethiourea), and the comet assay was performed. Twenty-four (77.42%) pesticides were present in the workers. The use of the maximum-likelihood factor analysis identified 8 different mixtures. Afterwards, robust regressions were used to explore associations between the factors identified and the comet assay. Two groups of mixtures- alpha-benzene hexachloride (alpha-BHC), hexachlorobenzene (HCB), and beta-BHC (beta: 1.21, 95% confidence interval [CI]: 0.33-2.10) and pirimiphos-methyl, malathion, bromophos-methyl, and bromophos-ethyl (beta: 11.97, 95% CI: 2.34-21.60)-were associated with a higher percentage of DNA damage and comet tail length, respectively. The findings suggest that exposure to pesticides varies greatly among rice field workers.","","","RefMan","","","","","","","","","",""
"Unknown","Unknown","Unknown","Unknown","","","1995","Venkat, J. A., Shami, S., Davis, K., Nayak, M., Plimmer, J. R., Pfeil, R., Nair, P. P.","Relative genotoxic activities of pesticides evaluated by a modified SOS microplate assay","Environmental and molecular mutagenesis","25(1):67-76","3dc3df8c-c291-4047-85cb-521b5b2b4c8d","","The genotoxic activities of 47 pesticides were determined using a modified SOS microplate assay in which the induction of beta-galactosidase in E. coli PQ37 was used as a quantitative measure of genotoxic activity. The results were compared with those obtained with anethole, curcumin, and capsaicin, a few examples of naturally occurring compounds present in foods. The assays were conducted with pesticides dissolved either in a suitable solvent, such as 10% DMSO in physiological saline or dispersed in sodium taurocholate micelles, to simulate conditions in the small intestine from where these substances are normally absorbed from the diet. 4-Nitroquinoline oxide (4-NQO) served as the reference standard of a direct acting mutagen. In micellar form, 4-NQO and 25 of the 47 pesticides tested showed significantly higher genotoxic activities than when they were tested in an organic solvent. In micellar form the SOS inducing potency of 4-NQO was almost twice as high as in 10% DMSO in physiological saline. In taurocholate micelles, the five most active compounds had activities in the range of 1,234-3,765 units/mumol and in the order of decreasing activities they were ranked as follows: malathion > dichlorvos > lindane > chlordane > endrin. They were significantly less active than 4-NQO (less than 40%). In micellar solution the naturally occurring compounds, anethole, curcumin, and capsaicin gave activities of 4,594, 928, and 809 units/mumol, respectively. These studies show that genotoxicity may depend upon the environment in which cells are exposed to these potential genotoxins. It appears that testing of the more hydrophobic compounds, both synthetic and naturally occurring, are needed.","","","RefMan","","","","","","","","","",""
"Unknown","Unknown","Unknown","Unknown","","","2015","Wagman, J. M., Achee, N. L., Grieco, J. P.","Insensitivity to the Spatial Repellent Action of Transfluthrin in Aedes aegypti: A Heritable Trait Associated with Decreased Insecticide Susceptibility","","9(4)","c8618fc9-c2f9-4eb6-8da5-edf866e80661","","Background: New vector control paradigms expanding the use of spatial repellents are promising, but

there are many gaps in our knowledge about how repellents work and how their long-term use might affect vector populations over time. Reported here are findings from a series of in vitro studies that investigated the plasticity and heritability of spatial repellent (SR) behaviors in Aedes aegypti exposed to airborne transfluthrin, including results that indicate a possible link between repellent insensitivity and insecticide resistance. Methodology/principal findings: A dual-choice chamber system was used to observe directional flight behaviors in Aedes aegypti mosquitoes exposed to passively emanating transfluthrin vapors (1.35 mg/m³). Individual SR responder and SR non-responder mosquitoes were identified, collected and maintained separately according to their observed phenotype. Subsequent testing included re-evaluation of behavioral responses in some mosquito cohorts as well as testing the progeny of selectively bred responder and non-responder mosquito strains through nine generations. At baseline (F<inf>0</inf> generation), transfluthrin actively repelled mosquitoes in the assay system. F<inf>0</inf> mosquitoes repelled upon initial exposure to transfluthrin vapors were no more likely to be repelled again by subsequent exposure 24h later, but repelled mosquitoes allowed to rest for 48h were subsequently repelled at a higher proportion than was observed at baseline. Selective breeding of SR responders for nine generations did not change the proportion of mosquitoes repelled in any generation. However, selective breeding of SR non-responders did produce, after four generations, a strain of mosquitoes that was insensitive to the SR activity of transfluthrin. Compared to the SR responder strain, the SR insensitive strain also demonstrated decreased susceptibility to transfluthrin toxicity in CDC bottle bioassays and a higher frequency of the V1016I^{kdr} mutation. Conclusions/significanceSR responses to volatile transfluthrin are complex behaviors with multiple determinants in Ae. aegypti. Results indicate a role for neurotoxic irritation of mosquitoes by sub-lethal doses of airborne chemical as a mechanism by which transfluthrin can produce SR behaviors in mosquitoes. Accordingly, how prolonged exposure to sub-lethal doses of volatile pyrethroids might impact insecticide resistance in natural vector populations, and how already resistant populations might respond to a given repellent in the field, are important considerations that warrant further monitoring and study. Results also highlight the critical need to develop new repellent active ingredients with novel mechanisms of action.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","1998","Walker, C. H.","The use of biomarkers to measure the interactive effects of chemicals","Ecotoxicology and environmental safety","40(1-2):65-70","f7dce0b6-eb11-424a-919b-7e4b68f55890","","Biomarker assays that provide measures of the toxic effects of chemicals on key organisms are of particular interest in ecotoxicology and environmental risk assessment. Typically, such assays provide measures of the molecular mechanisms that underlie toxicity (e.g., inhibition of brain acetylcholinesterase activity by organophosphorus insecticides and retardation of the vitamin K cycle by anticoagulant rodenticides). They are particularly valuable for detecting and quantifying toxicity where organisms are exposed to mixtures of compounds and for identifying cases of potentiation. In birds, inhibition of brain acetylcholinesterase activity can provide an index of potentiation of organophosphorus and carbamate insecticides by other pesticides. Inhibition of serum butyrylcholinesterase also is very useful as a nondestructive assay but is not simply related to inhibition of brain acetylcholinesterase. Assays for DNA damage can indicate where there is an increase in the rate of activation of carcinogens and mutagens due to induction of the cytochrome

P450 system. Assays for blood levels of retinol (vitamin A) and thyroxine can establish thyroxine antagonism by metabolites of 3,3,4,4-tetrachlorobiphenyl. Assays for changes in levels of clotting protein in serum can give an indication of the effect of mixtures of anticoagulant rodenticides on the vitamin K cycle. The interactive effects of mixtures of pesticides in the field are starting to be investigated by this approach (e.g., a recent study of the combined action of malathion and prochloraz in the red-legged partridge).","","","RefMan","","","","","","","","","" "Unknown","Unknown","Unknown","Unknown","","","1998","Windham, G. C., Titenko-Holland, N., Osorio, A. M., Gettner, S., Reinisch, F., Haas, R., Smith, M.","Genetic monitoring of malathion-exposed agricultural workers","American journal of industrial medicine","33(2):164-74","abdac031-b20a-45a4-82c3-7b579e7af1e9","","The aerial application of malathion over large urban populations in Southern California during the early 1990s raised concerns about adverse health effects, including the potential to cause genetic damage. Workers in the Mediterranean fruit fly eradication program, which involved application of malathion as ground treatment, were studied to examine micronucleus formation and mutation frequencies assessed by the glycophorin A (GPA) assay. In the 1992 pilot project the mean micronuclei level appeared higher in lymphocytes of exposed workers (n = 13) compared to controls (n = 4) (20.1 +/- 7.1 vs 14.3 +/- 7.2 respectively, P = 0.09). During the 1993 season, neither of the cohorts examined showed a higher level of micronuclei in workers exposed to malathion compared to unexposed, nor did the pooled total (n = 53; means = 17.8 +/- 7.2 vs 18.5 +/- 6.3, respectively), even after adjustment by multiple regression. The GPA variant frequency was not associated with malathion exposure in any of the cohorts. These results suggest that any potential risk of genotoxic damage from exposure to malathion is relatively low, but other assays may be more sensitive, and the sample size was small.","","","RefMan","","","","","","","","","" "Unknown","Unknown","Unknown","Unknown","","","2015","Yanola, J., Chamnanya, S., Lumjuan, N., Somboon, P.","Insecticides resistance in the Culex quinquefasciatus populations from northern Thailand and possible resistance mechanisms","Acta tropica","149:232-8","d0fbe166-121d-403a-a225-383d5fac78be","","The mosquito vector Culex quinquefasciatus is known to be resistant to insecticides worldwide, including Thailand. This study was the first investigation of the insecticide resistance mechanisms, involving metabolic detoxification and target site insensitivity in C. quinquefasciatus from Thailand. Adult females reared from field-caught larvae from six provinces of northern Thailand were determined for resistant status by exposing to 0.05% deltamethrin, 0.75% permethrin and 5% malathion papers using the standard WHO susceptibility test. The overall mortality rates were 45.8%, 11.4% and 80.2%, respectively. A fragment of voltage-gated sodium channel gene was amplified and sequenced to identify the knock down resistance (kdr) mutation. The ace-1 gene mutation was determined by using PCR-RFLP. The L1014F kdr mutation was observed in all populations, but the homozygous mutant F/F1014 genotype was found only in two of the six provinces where the kdr mutation was significantly correlated with deltamethrin resistance. However, none of mosquitoes had the G119S mutation in the ace-1 gene. A laboratory deltamethrin resistant strain, Cq_CM_R, has been established showing a highly resistant level after selection for a few generations. The mutant F1014 allele frequency was significantly increased after one generation of selection. A synergist assay was performed to assess the metabolic detoxifying enzymes. Addition of bis(4-nitrophenyl)-phosphate (BNPP) and diethyl maleate (DEM), inhibitors of esterases and

glutathione S-transferases (GST), respectively, into the larval bioassay of the Cq_CM strain with deltamethrin showed no significant reduction. By contrast, addition of piperonyl butoxide (PBO), an inhibitor of cytochrome P450 monooxygenases, showed a 9-fold reduction of resistance. Resistance to pyrethroids in C. quinquefasciatus is widely distributed in northern Thailand. This study reports for the first time for the detection of the L1014F kdr mutation in wild populations of C. quinquefasciatus in Thailand. At least two major mechanisms, kdr and cytochrome P450 monooxygenases, confer resistance to deltamethrin in Thai C. quinquefasciatus populations.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","2011","Yewhalaw, D., Wassie, F., Steurbaut, W., Spanoghe, P., Van Bortel, W., Denis, L., Tessema, D. A., Getachew, Y., Coosemans, M., Duchateau, L., Speybroeck, N.","Multiple insecticide resistance: an impediment to insecticide-based malaria vector control program","PloS one","6(1):e16066","39ed66bb-65cc-4d1f-9d1e-24266733f796","","BACKGROUND: Indoor Residual Spraying (IRS), insecticide-treated nets (ITNs) and long-lasting insecticidal nets (LLINs) are key components in malaria prevention and control strategy. However, the development of resistance by mosquitoes to insecticides recommended for IRS and/or ITNs/LLINs would affect insecticide-based malaria vector control. We assessed the susceptibility levels of Anopheles arabiensis to insecticides used in malaria control, characterized basic mechanisms underlying resistance, and evaluated the role of public health use of insecticides in resistance selection. METHODOLOGY/PRINCIPAL FINDINGS: Susceptibility status of An. arabiensis was assessed using WHO bioassay tests to DDT, permethrin, deltamethrin, malathion and propoxur in Ethiopia from August to September 2009. Mosquito specimens were screened for knockdown resistance (kdr) and insensitive acetylcholinesterase (ace-1(R)) mutations using AS-PCR and PCR-RFLP, respectively. DDT residues level in soil from human dwellings and the surrounding environment were determined by Gas Chromatography with Electron Capture Detector. An. arabiensis was resistant to DDT, permethrin, deltamethrin and malathion, but susceptible to propoxur. The West African kdr allele was found in 280 specimens out of 284 with a frequency ranged from 95% to 100%. Ace-1(R) mutation was not detected in all specimens scored for the allele. Moreover, DDT residues were found in soil samples from human dwellings but not in the surrounding environment. CONCLUSION: The observed multiple-resistance coupled with the occurrence of high kdr frequency in populations of An. arabiensis could profoundly affect the malaria vector control programme in Ethiopia. This needs an urgent call for implementing rational resistance management strategies and integrated vector control intervention.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","2009","Yi, O.","Cytogenetic study on workmen occupationally exposed to pesticides","","12(1):51-59","b24f0c0e-fc52-47aa-8827-416c11e98a2c","","A cytogenetic study was performed on 40 workmen who were exposed to the pesticides malathion and chlorpyrifos and on 30 healthy males who had not been so exposed. The exposed workers had a consistent increase in chromosome abnormalities including chromatid gap, chromatid break, isochromatid break, dicentric and ring chromosomes, as determined by the standard chromosome aberration assay, when compared to the control group. The incidence was significantly higher in exposed smokers than that for exposed non smokers and than that for the unexposed controls as well. These findings provide further evidence for the intrinsic mutagenic activity of the pesticides studied.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","2003","Yoon, K. S., Gao, J. R., Lee, S.

H., Clark, J. M., Brown, L., Taplin, D.","Permethrin-resistant human head lice, Pediculus capitis, and their treatment","Archives of dermatology","139(8):994-1000","f2d9f150-8159-40aa-b5c8-42f52c406f60","","OBJECTIVE: To compare the pediculicidal activity of Ovide lotion and its active ingredient, 0.5% malathion, with Nix and its active ingredient, 1% permethrin, in permethrin-resistant head lice. DESIGN: In vitro pediculicidal product and active ingredient comparison. The presence of knockdown resistance-type mutations (T929I and L932F) was validated by DNA sequencing. SETTING: University of Massachusetts-Amherst; University of Miami School of Medicine, Miami, Fla; Plantation and Homestead, Fla; and Mathis, Tex. OTHER PARTICIPANTS: Lice were collected in 3 geographical regions within the United States and in Yamburara, Ecuador, from healthy but infested individuals. Intervention Within 3 to 6 hours of collection, lice were given a blood meal, exposed to products or active ingredients, and observed at regular intervals. MAIN OUTCOME MEASURES: Percent mortality of lice at regular intervals after exposure to products or active ingredients and presence of T929I and L932F mutations. RESULTS: South Florida lice exhibited a significantly slower mortality response to permethrin compared with susceptible Ecuadorian lice. Ovide and malathion killed permethrin-resistant lice faster than Nix or permethrin. The presence of T929I and L932F in permethrin-resistant south Florida lice was confirmed by DNA sequencing. The population of Texas lice from Mathis was slightly resistant to permethrin and included 13% with resistant genotypes. CONCLUSIONS: The presence of the T929I and L932F mutations was confirmed by DNA sequencing in lice collected from children in south Florida that were resistant to the pediculicidal effects of permethrin and the leading permethrin-based head lice product, Nix. Malathion resistance was not observed in this study. The data also show that Ovide killed these same permethrin-resistant head lice approximately 10 times faster than permethrin or Nix.","","","RefMan","","","","","","","","","" "Unknown","Unknown","Unknown","Unknown","","","2009","Yu, Q., Abdallah, I., Han, H., Owen, M., Powles, S.","Distinct non-target site mechanisms endow resistance to glyphosate, ACCase and ALS-inhibiting herbicides in multiple herbicide-resistant Lolium rigidum","Planta","230(4):713-23","aaefbe4e-096e-437a-90dd-d718af839c20","","This study investigates mechanisms of multiple resistance to glyphosate, acetyl-coenzyme A carboxylase (ACCase) and acetolactate synthase (ALS)-inhibiting herbicides in two Lolium rigidum populations from Australia. When treated with glyphosate, susceptible (S) plants accumulated 4- to 6-fold more shikimic acid than resistant (R) plants. The resistant plants did not have the known glyphosate resistance endowing mutation of 5-enolpyruvylshikimate-3 phosphate synthase (EPSPS) at Pro-106, nor was there over-expression of EPSPS in either of the R populations. However, [(14)C]-glyphosate translocation experiments showed that the R plants in both populations have altered glyphosate translocation patterns compared to the S plants. The R plants showed much less glyphosate translocation to untreated young leaves, but more to the treated leaf tip, than did the S plants. Sequencing of the carboxyl transferase domain of the plastidic ACCase gene revealed no resistance endowing amino acid substitutions in the two R populations, and the ALS in vitro inhibition assay demonstrated herbicide-sensitive ALS in the ALS R population (WALR70). By using the cytochrome P450 inhibitor malathion and amitrole with ALS and ACCase herbicides, respectively, we showed that malathion reverses chlorsulfuron resistance and amitrole reverses diclofop resistance in the R population examined. Therefore, we conclude that multiple glyphosate, ACCase and ALS herbicide resistance in the two R populations is due to the presence of

distinct non-target site based resistance mechanisms for each herbicide. Glyphosate resistance is due to reduced rates of glyphosate translocation, and resistance to ACCase and ALS herbicides is likely due to enhanced herbicide metabolism involving different cytochrome P450 enzymes.","","","RefMan","","","","","","","","","" "Unknown","Unknown","Unknown","Unknown","","","2011","Zhang, X., Wallace, A., Du, P., Baccarelli, A., Jafari, N., Lin, S., Hou, L.","Genome-wide study of DNA methylation alterations in response to pesticide exposure in in vitro","","71(8)","a16242e3-655d-42ce-ac4e-c0f719960e39","","Pesticides are widely used in the US and worldwide, and are pervasive in our environment. All pesticides sold in the US have passed the Environmental Protection Agency (EPA) screening procedures for carcinogenicity based on their genotoxicity and mutagenicity. However exposure to pesticides among pesticide applicators and manufacturing workers has repeatedly been shown to increase cancer risk, suggesting that pesticides may cause cancer via alternative mechanisms, such as epigenetic changes. The purpose of the present study is to examine whether exposure to organophosphate pesticides (OPs), a group of the most commonly used pesticides in the US, induces DNA methylation alterations in in-vitro. The K562 progenitor blood cell line was exposed to several OPs (i.e., chlorpyrifos, diazinon, fonofos, malathion, parathion, phorate, and terbufos) at different dosages and time periods. DNA was prepared from samples exposed to ethanol (control) and a range of pesticide concentrations similar to exposure levels experienced by the US licensed pesticide applicators. We conducted genomewide DNA methylation analysis using the Illumina Infinium HumanMethylation27 BeadChip that covers 27,578 individual promoter CpG sites in the entire genome. The relative level of methylation was calculated as the ratio of signal from a methylated probe relative to an unmethylated probe. Bayesian-adjusted t-tests were used to identify differentially methylated sites. A cut-off of False Discovery Rate (FDR)-adjusted p-value (q-value) < 0.05 and fold change > 2 was used to identify candidate CpG sites. We observed significant differences in genomewide DNA methylation patterns in relation to exposure to three pesticides (i.e., fonofos, parathion, and terbufos) that have been associated with cancers in human studies. Out of all genes with differentially methylated CpG site(s) for each of the three pesticides, we identified 712 genes (625 were hypermethylated and 87 were hypomethylated) overlapped for these three pesticides. Gene ontology analysis showed that these hyper- or hypo-methylated genes are implicated in carcinogenesis and related biological process, such as tumor protein p53 inducible protein 11 (TP53I11) (4.0-fold for fonofos, 4.7-fold for parathion, 3.1-fold for terbufos, respectively), growth arrest and DNA-damage-inducible gamma (GADD45G) (25.2-fold for fonofos, 23.1-fold for parathion, 31.2-fold for terbufos, respectively), and interleukin-1 receptor (IL1R1) (-2.2-fold for fonofos, -2.1-fold for parathion, -2.2 fold for terbufos, respectively). Our results provided direct experimental evidence that pesticides can modify DNA methylation in gene promoter CpG sites, which may play pathological role in cancer development. Further studies in other cell types and human samples are required before any firm conclusion could be reached on the significance of pesticide-induced methylation.","","","RefMan","","","","","","","","","" "Unknown","Unknown","Unknown","Unknown","","","2012","Zhang, X., Wallace, A. D., Du, P., Kibbe, W. A., Jafari, N., Xie, H., Lin, S., Baccarelli, A., Soares, M. B., Hou, L.","DNA methylation alterations in response to pesticide exposure in vitro","Environmental and molecular mutagenesis","53(7):542-9","ac364b88-9074-48c3-9d2d-ef703ab41cb0","","Although pesticides are subject to extensive carcinogenicity

testing before regulatory approval, pesticide exposure has repeatedly been associated with various cancers. This suggests that pesticides may cause cancer via nonmutagenicity mechanisms. The present study provides evidence to support the hypothesis that pesticide-induced cancer may be mediated in part by epigenetic mechanisms. We examined whether exposure to seven commonly used pesticides (i.e., fonofos, parathion, terbufos, chlorpyrifos, diazinon, malathion, and phorate) induces DNA methylation alterations in vitro. We conducted genome-wide DNA methylation analyses on DNA samples obtained from the human hematopoietic K562 cell line exposed to ethanol (control) and several organophosphate pesticides (OPs) using the Illumina Infinium HumanMethylation27 BeadChip. Bayesian-adjusted t-tests were used to identify differentially methylated gene promoter CpG sites. In this report, we present our results on three pesticides (fonofos, parathion, and terbufos) that clustered together based on principle component analysis and hierarchical clustering. These three pesticides induced similar methylation changes in the promoter regions of 712 genes, while also exhibiting their own OP-specific methylation alterations. Functional analysis of methylation changes specific to each OP, or common to all three OPs, revealed that differential methylation was associated with numerous genes that are involved in carcinogenesis-related processes. Our results provide experimental evidence that pesticides may modify gene promoter DNA methylation levels, suggesting that epigenetic mechanisms may contribute to pesticide-induced carcinogenesis. Further studies in other cell types and human samples are required, as well as determining the impact of these methylation changes on gene expression.","","","RefMan","","","","","","","","","","","Unknown","Unknown","Unknown","Unknown","","","1999","Zhu, Y. C., Dowdy, A. K., Baker, J. E.","Differential mRNA expression levels and gene sequences of a putative carboxylesterase-like enzyme from two strains of the parasitoid Anisopteromalus calandrae (Hymenoptera: Pteromalidae)","Insect biochemistry and molecular biology","29(5):417-25","3811ba4b-63cf-4e53-8c7f-a3893bf0ae72","","Carboxylesterase-like enzyme cDNAs have been cloned and sequenced from malathion-resistant and susceptible strains of the parasitoid Anisopteromalus calandrae (Howard) (Hymenoptera: Pteromalidae). The cDNAs consist of 1963 nucleotides including a 35 bp untranslated 5'-end, a 1596 bp open reading frame, and a 332 bp untranslated 3'-end. The open reading frame encodes 532 amino acid residues. The predicted protein sequence from these cDNAs includes 2 potential N-glycosylation sites, a carboxylesterase type-B serine active site FGGDSENVTIFGESAG, and conserved residues Ser187, Glu317, and His432 to function as the catalytic triad. The predicted carboxylesterase-like enzyme sequence is most similar to that of the carboxylesterase from the peach-potato aphid, Myzus persicae with 45% sequence identity. Alignment of the parasitoid carboxylesterase-like enzyme cDNAs revealed that there are two nucleotide differences in the open reading frame between the parasitoid strains, including a silent mutation and a point mutation that presumably causes a gene product difference. A nucleotide thymine at position 658 in the susceptible strain cDNA is replaced by a guanine in the resistant strain cDNA. This substitution leads to an amino acid change from tryptophan (Trp220) in the susceptible strain to glycine (Gly220) in the resistant strain. This substitution is genetically linked to resistance but it is not known how or if this amino acid substitution affects detoxification of malathion. Northern blot analyses demonstrated that expression level of the carboxylesterase-like enzyme mRNA in adult A. calandrae is approximately 30-fold higher in the resistant strain relative to that in the susceptible strain. Southern

analysis indicated that Pst I or Eco RI restriction sites are different in the two strains. Both a modified gene structure and an increase in expression of carboxylesterase may be responsible for the high level of resistance found in this beneficial wasp.","","","RefMan","","","","","","","","","","
"Unknown","Unknown","Unknown","Unknown","","","2004","Zhu, Y. C., Snodgrass, G. L., Chen, M. S.","Enhanced esterase gene expression and activity in a malathion-resistant strain of the tarnished plant bug, Lygus lineolaris","Insect biochemistry and molecular biology","34(11):1175-86","73eb6d51-6e4b-4da3-abab-c0c8d46ece0d","","Extensive use of insecticides on cotton in the mid-South has prompted resistance development in the tarnished plant bug, Lygus lineolaris (Palisot de Beauvois). A field population of tarnished plant bugs in Mississippi with 11-fold higher resistance to malathion was used to examine how gene regulation conferred resistance to this organophosphate insecticide. In laboratory bioassays, synergism by the esterase inhibitors S,S,S,-tributylphosphorotrithioate (DEF) and triphenylphosphate (TPP) effectively abolished resistance and increased malathion toxicity by more than 80%. Esterase activities were compared in vitro between malathion susceptible and resistant (selected) strains. More than 6-, 3- and 10-fold higher activities were obtained with the resistant strain using alpha-naphthyl acetate, beta-naphthyl acetate, and p-nitrophenyl acetate, respectively. Up to 95% and 89% of the esterase activity in the susceptible and resistant strains, respectively, was inhibited by 1 mM DEF. Inhibition of esterase activity up to 75% and 85% in the susceptible and resistant strains, respectively, was obtained with 0.03 mM TPP. Esterase activities in field populations increased by up to 5.4-fold during the fall season. The increase was synchronized with movement of the insect into cotton where exposure to pesticides occurred. Esterase cDNA was cloned and sequenced from both malathion susceptible and resistant strains. The 1818-nucleotide cDNA contained a 1710-bp open reading frame coding a 570 amino acid protein which was similar to many insect esterases conferring organophosphate resistance. No amino acid substitution was observed between susceptible and resistant strains, indicating that esterase gene mutation was not involved in resistance development in the resistant strain in Mississippi. Further examination of esterase gene expression levels using quantitative RT-PCR revealed that the resistant strain had a 5.1-fold higher level of esterase mRNA than the susceptible strain. The results of this study indicated that up-regulation of the esterase gene appeared to be related to the development of resistance in the tarnished plant bug.","","","RefMan","","","","","","","","","","